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TETRAACYLOXYSILANES IN ORGANIC SYNTHESIS

XIII. SYNTHESIS OF N,N-DIETHYLAMIDES AND N-ARYLAMIDES OF ACIDS WITH THE AID OF SILICOANHYDRIDES OF SATURATED MONOBASIC ORGANIC ACIDS

Iu. K. Iur'ev and Z. V. Beliakova

N-Substituted amides of organic acids are usually prepared by the reaction of alkyl amines and anhydrides or acid chlorides of the appropriate acids, whereby only 50% of the alkyl amine can be utilized for the production of the N-alkyl- or N,N-dialkylamide of the acid, since the remaining 50% is consumed in the formation of a second reaction product— the salt of the amine. Thus, when diethyl amine is reacted with acetic anhydride, N,N-diethylacetamide [1] and diethylamine acetate are obtained. When diethyl amine reacts with acetyl chloride, propionyl chloride, and butyryl chloride, the corresponding N,N-diethylamides of acetic [2], propionic [3], and butyric [2, 4] acids and diethylamine hydrochloride are obtained.

The N,N-diethylamides of the acids are also prepared directly from the acids and diethylamine by heating to 230°. In this way the N,N-diethylamides of acetic [5] and isovaleric [6] acids have been prepared. A series of aliphatic N,N-dimethylamides [7] has been prepared with yields of 70-80% by heating a mixture of the acid and dimethylamine to 200° in an autoclave.

The last method, however, does not always permit attaining good yields, and for this reason recourse is had more frequently to the preparation of the N,N-diethylamides from the acid chlorides.

N-Arylamides, as is well known, can be prepared directly from the acid and aniline; however, not infrequently the anhydrides [8, 9] and acid chlorides [10, 11] of the acids are also used for the preparation of the anilides.

In the present work we used tetraacyloxysilanes— mixed anhydrides of orthosilicic and organic acids— for the preparation of N,N-diethylamides and N-arylamides. These had been used successfully in place of the anhydrides and acid chlorides of the acids by K. D. Petrov [12] for the acylation of aromatic compounds (benzene and toluene) and by us for the acylation of heterocyclic compounds— thiophene [13], selenophene [14], pyrrole and indole [15], and also for the synthesis of aromatic α,β-unsaturated acids [16].

It should be noted that it is indicated in the literature by Friedel and Ladenburg that acetamide is formed by the reaction of ammonia with the silicoanhydride of acetic acid [17].

Having shown previously that tetraacyloxysilanes enter into all the reactions that are characteristic of acid anhydrides, although less actively [18], we reacted the silicoanhydrides of acetic, propionic, n-butyric, n-valeric, isovaleric, and n-caproic acids with diethylamine and obtained good yields (60-90%) of the corresponding N,N-diethylamides of acetic, propionic, n-butyric, n-valeric, isovaleric, and n-caproic acids:

$$(RCOO)_4Si + 4NH(C_2H_5)_2 \rightarrow 4RCON(C_2H_5)_2 + Si(OH)_4$$

(R=CH_3, C_2H_5, C_3H_7, n-C_4H_9, iso-C_4H_9, C_5H_{11})

When aniline was reacted with tetraacetoxysilane, acetanilide was obtained in 90% yield.

$$4C_6H_5NHR' + (CH_3COO)_4Si \rightarrow 4C_6H_5\overset{\displaystyle R'}{\underset{|}{N}}—COCH_3 + Si(OH)_4,$$

where R' = H, CH_3

The method proposed by us for the preparation of amides and arylamides of acids by the reaction of amines with tetraacyloxysilanes is convenient because, first, tetraacyloxysilanes are very easily prepared from silicon tetrachloride and the appropriate acids in benzene and do not require any purification before use, and second, because in this reaction all the amine should go into the formation of the corresponding substituted amide.

EXPERIMENTAL

Methods of Preparing N,N-Diethylamides

In a 250-ml three-necked flask, fitted with a stirrer, a reflux condenser with a calcium chloride tube, and a gas delivery tube reaching to the bottom of the flask, was placed 100 ml of anhydrous benzene, 0.15 g-mole of organic, saturated, monobasic acid, and 0.045 g mole of silicon tetrachloride, and the mixture was heated on a water bath first at 60-70° and then to boiling, until the evolution of hydrogen chloride completely ceased. To completely remove the hydrogen chloride from the mixture, a stream of dry air was passed through it for 15-20 minutes. The mixture was cooled with ice water, the gas delivery tube was replaced by a dropping funnel, and 0.1 g-mole of diethylamine was added drop by drop. The reaction mixture thereupon heated up and often a precipitate of silicic acid separated out immediately. When all the amine had been introduced, stirring of the mixture was continued for 1 hour at room temperature and then it was heated for 4-5 hours on a water bath, first at 40-50° and afterward to boiling. The mixture was cooled and the precipitate of silicic acid was filtered off and washed with benzene. The combined benzene solution was washed with 2 N sodium hydroxide solution, dried with anhydrous sodium sulfate and, after the benzene was distilled off, the residue was distilled in vacuo. The yield of N,N-diethylamide obtained was calculated on the basis of the diethylamine used in the reaction.

N,N-Diethylacetamide. Using an acetic acid: diethylamine ratio of 1.5:1, we obtained from 9 g of acetic acid, 5.2 ml of silicon tetrachloride, and 7.3 g of diethylamine 9.6 g (83.5%) of N,N-diethylacetamide; b. p. 88-89° (26 mm).

With an acetic acid: diethylamine ratio of 1:1, we obtained from 9 g of acetic acid, 5.2 ml of silicon tetrachloride, and 10.95 g of diethylamine 10.45 g (60.5%) of N,N-diethylacetamide; b. p. 93-94° (35 mm).

With an acetic acid: diethylamine ratio of 2:1, we obtained from 12 g of acetic acid, 7 ml of silicon tetrachloride, and 7.3 g of diethylamine 10.4 g (90%) of N,N-diethylacetamide; b. p. 93-94° (35 mm).

The N,N-diethylacetamide thus obtained had the following constants: b. p. 93-94° (35 mm), n_D^{20} 1.4401, d_4^{20} 0.9048, MR_D 33.55; calc. 33.53.*

Found %: N 12.22, 12.35. $C_6H_{13}ON$. Calculated %: N 12.16.

Literature data: b. p. 184-184.8° (747 mm); n_D^{20} 1.4396; d_4^{20} 0.9045 [19].

N,N-Diethylpropionamide. From 11.1 g (0.15 g-mole) of propionic acid, 5.2 ml (0.045 g-mole) of silicon tetrachloride, and 7.3 g (0.1 g-mole) of diethylamine we obtained 11.5 g (89%) of N,N-diethylpropionamide: b. p. 77° (12 mm), n_D^{20} 1.4419, d_4^{20} 0.8972, MR_D 38.12; calc. 38.15.

Found %: N 11.14, 11.21. $C_7H_{15}ON$. Calculated %: N 10.84.

Literature data: b. p. 191° [3].

*In the calculation of the additive values of MR_D for N,N-diethylacetamide and the N,N-diethylamides of the other acids obtained in our work, the atomic refraction of nitrogen was taken as 2.508, the value established by B. V. Ioffe for tertiary amides (except formamides) [19].

N,N-Diethylbutyramide. From 13.3 g (0.15 g-mole) of n-butyric acid, 5.2 ml (0.045 g-mole) of silicon tetrachloride, and 7.3 g (0.1 g-mole) of diethylamine we obtained 12.85 g (90%) of N,N-diethylbutyramide:

b. p. 79-80° (8 mm), n_D^{20} 1.4431, d_4^{20} 0.8884, MR_D 42.75; calc. 42.76.

Found %: N 9.96, 10.01. $C_8H_{17}ON$. Calculated %: N 9.78.

Literature data: b. p. 206°, 106° (24 mm), 92° (12 mm) [4].

N,N-Diethylvaleramide. From 15.3 g (0.15 g-mole) of n-valeric acid, 5.2 ml (0.045 g-mole) of silicon tetrachloride, and 7.3 g (0.1 g-mole) of diethylamine we obtained 12.45 g (79%) of N,N-diethylvaleramide:

b. p. 94-95° (10 mm), n_D^{20} 1.4452, d_4^{20} 0.8808, MR_D 47.53; calc. 47.38.

Found %: N 9.18, 9.29. $C_9H_{19}ON$. Calculated %: N 8.91.

N,N-Diethylvaleramide is not described in the literature.

N,N-Diethylisovaleramide. From 15.3 g (0.15 g-mole) of isovaleric acid, 5.2 ml (0.045 g-mole) of silicon tetrachloride, and 10.95 g (0.15 g-mole) of diethylamine we obtained 16.15 g (70%) of N,N-diethylisovaleramide:

b. p. 77-78° (5 mm), n_D^{20} 1.4422, d_4^{20} 0.8764, MR_D 47.5; calc. 47.38.

Found %: N 9.06, 9.11. $C_9H_{19}ON$. Calculated %: N 8.91.

Literature data: b. p. 93-95° (14 mm) [21].

N,N-Diethylcaproamide. From 17.4 g (0.15 g-mole) of n-caproic acid, 5.2 ml (0.045 g-mole) of silicon tetrachloride, and 10.95 g (0.15 g-mole) of diethylamine we obtained 14.55 g (61%) of N,N-diethylcaproamide:

b. p. 95-96° (5 mm), n_D^{20} 1.4467, d_4^{20} 0.8784, MR_D 52.07; calc. 52.00.

Found %: N 8.48, 8.41. $C_{10}H_{21}ON$. Calculated %: N 8.18.

N,N-Diethylcaproamide is not described in the literature.

Acetanilide. To a cooled benzene solution of silicoacetic anhydride prepared as described above from 12 g (0.2 g-mole) of acetic acid and 7 ml (0.06 g-mole) of silicon tetrachloride, there was added with continuous stirring, drop by drop, 9.3 g (0.1 g-mole) of aniline in 30 ml of anhydrous benzene. The reaction mixture was heated on a boiling water bath for 10 hours, and the precipitate of silicic acid that had separated was filtered off and washed with hot benzene. The crystals of acetanilide that precipitated when the benzene solution was cooled were filtered off. When the benzene had been distilled off from the mother liquor, more crystals of acetanilide were obtained, which were recrystallized from water. Yield 12.2 g (90%); m. p. 115°.

A mixed melting point test with known acetanilide showed no depression.

Literature data: m. p. 115° [22].

N-Methylacetanilide. The synthesis was carried out as described for acetanilide. The precipitate of silicic acid was filtered off, washed with hot benzene, and when the benzene had been distilled off from the combined filtrates, the remaining crystals were pressed out on a porous plate. From 12 g (0.2 g- mole) of acetic acid, 7 ml (0.06 g-mole) of silicon tetrachloride, and 10.7 g (0.1 g-mole) of N-methylaniline we obtained 13.4 g (90%) of N-methylacetanilide with m. p. 102° (from alcohol). A mixed melting point with known N-methylacetanilide showed no depression.

Literature data: m. p. 101-102° [10].

SUMMARY

Reaction of silicoanhydrides of saturated, monobasic, organic acids with secondary aliphatic amines may serve as a convenient method for the synthesis of N,N-dialkylamides of the acids. By this method the N,N-diethylamides of acetic, propionic, n-butyric, n-valeric, isovaleric, and caproic acids were prepared in good yields (60-90%).

The possibility of preparing N-arylamides in this way was demonstrated by the examples of the acylation of aniline and methylaniline with silicoacetic anhydride.

In the synthesis of N-substituted amides of acids, the use of tetraacyloxysilanes has the advantage over the use of the acid chlorides or the anhydrides of the acids.

LITERATURE CITED

[1] A. Pitet, Ber. 23, 3013 (1890).

[2] A. Hildebrandt, Arch. Exp. Pathologie u. Pharmazie, 54, 129 (1906).

[3] I. Braun, Ber. 36, 2287 (1903).

[4] M. Montagne, Ann. Chim. phys. [10], 13, 53 (1930).

[5] L. Musselius, J. Russ. Phys. Chem. Soc. 32, 29 (1900).

[6] German Patent 129,967 (1902).

[7] J. Ruhoff and E. Reid, J. Am. Chem. Soc. 59, 4012 (1937).

[8] A. Kaufmann, Ber. 42, 3481 (1909).

[9] G. Morgan and W. Grist, J. Chem. Soc. 113, 691 (1918).

[10] P. Hepp, Ber. 10, 329 (1877).

[11] Ch. Gerhardt, Lieb. Ann. 87, 164 (1853).

[12] K. D. Petrov and M. I. Itkina, J. Gen. Chem. 17, 220 (1947).

[13] Iu. K Iur'ev and G. B. Eliakov, Proc. Acad. Sci. USSR, 86, 337 (1952).

[14] Iu. K. Iur'ev and G. B. Eliakov, Proc. Acad. Sci. USSR 102, 763 (1955).

[15] Iu. K. Iur'ev and G. B. Eliakov, J. Gen. Chem. 26, 2350 (1956).*

[16] Iu. K. Iur'ev, G. B. Eliakov and A. N. Vysokosov, J. Gen. Chem. 26, 926 (1956).*

[17] C. Friedel and A. Ladenburg, Lieb. Ann. 145, 174 (1868).

[18] Iu. K. Iur'ev, Z. V. Beliakova and N. S. Zefirov, J. Gen. Chem. 27, 3260 (1957).*

[19] B. V. Ioffe, J. Gen. Chem. 25, 902 (1955).*

[20] J. Braun and A. Heymons, Ber. 62, 411 (1929).

[21] M. Hamell and R. Levine, J. Org. Ch. 15, 163 (1950).

[22] H. Inoue, Bull. Chim. Soc. Japan, 1, 177 (1926); Zbl. 1926, II, 2711.

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CATALYTIC CONVERSIONS OF HETEROCYCLIC COMPOUNDS

LIII. CONVERSION OF HOMOLOGS OF OXAZOLE TO HOMOLOGS OF THIAZOLE

Iu. K. Iur'ev and I. G. Zhukova

In spite of the existence of a deep-seated difference in the chemical nature of compounds of the furan series and the oxazole series, which is manifested, for example, in the almost complete absence of acidophobic properties in the oxazoles and clearly expressed acidophobic properties in the furans, the oxazoles also display a number of characteristics that are typical of the furans and are explained by the structural similarity of these heterocyclic systems.

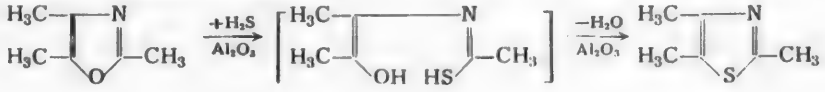
Thus, the replacement of a cyclically bound oxygen atom by an imino group characteristic of the furans—the conversion of furan and its homologs by the action of ammonia or amines to pyrrole [1] and N-substituted pyrroles — finds a complete analogy in the very easy formation of imidazoles from oxazoles. Compounds of the oxazole series are converted into imidazoles by heating with alcoholic [2] or aqueous ammonia solution [3] or by heating with formamide [4]; the reaction of oxazoles with aniline [2] also proceeds very readily and results in the formation of N-phenylimidazoles.

The reaction of oxazoles with hydrogen sulfide, which should lead to the formation of the corresponding thiazoles, has not been investigated; the conversion, recently described in the literature, of 2-methyl-4-isopropylideneoxazolone-5 to 2,5,5-trimethylthiazoline-4-carboxylic acid by the action of hydrogen sulfide [5] cannot serve as an example of the conversion of the parent oxazole ring to the thiazole ring, since it is the result of a more complex change in the molecule.

But the reaction of oxazole and its homologs with hydrogen sulfide presents considerable interest with respect to the characteristics of the oxazole ring: the formation of thiazoles from oxazoles in this reaction would be a complete confirmation of the chemical similarity of these structurally close cyclic systems with their cyclically bound oxygen atom.

A study carried out by us of the catalytic conversion of methyl homologs of oxazole by the action of hydrogen sulfide showed that the alkyloxazoles, like other five- and six-membered oxygen-containing heterocyclic compounds, both of aromatic nature and saturated, undergo this general reaction of replacement of cyclically bound oxygen by sulfur. As a result of the action of hydrogen sulfide in the presence of aluminum oxide on 2,4-, 2,5-, and 4,5-dimethyloxazole, and also 2,4,5-trimethyloxazole, they are converted respectively to 2,4-, 2,5-, and 4,5-dimethylthiazole and 2,4,5-trimethylthiazole. As also in the case of the conversion of furan to thiophene, the conversion of the oxazole ring proceeds, no doubt, through the intermediate stage of formation of the 1,4-mercaptohydroxy compound, by the dehydration of which the thiazole ring originates.

It should be noted that the yield of the methyl homologs of thiazole was small and amounted in all to 10-15%, while it was possible to isolate from the products of catalysis only up to 20% of unchanged alkyloxazole, and the catalyst was covered with a thick incrustation of carbonaceous deposit — products of deep-seated decomposition of the alkyloxazole molecule.



The presence of unchanged alkyloxazole in the products of catalytic conversion by the action of hydrogen sulfide is evidence, on the one hand, of the stability of the oxazole ring to the action of a reagent of acid character and, on the other hand, of the comparatively slight stability of this ring on contact with aluminum oxide heated to 300-375°. A suggestion concerning the possible reversibility of the reaction — oxazole + H_2S ⇌ thiazole + H_2O — was not confirmed: in the catalyzate obtained by passing a mixture of 4,5-dimethylthiazole and steam over aluminum oxide at 375° 4,5-dimethyloxazole was not found.

Comparison of the results obtained by the synthesis described in the literature of imidazoles from substituted oxazoles with the results obtained by us in the catalytic conversion of oxazoles to thiazoles shows that replacement of the cyclically bound oxygen atom in oxazole homologs by the imino group or sulfur depends in great degree on the chemical nature of the reagent under the influence of which this exchange takes place (ammonia, alkylamines, arylamines, hydrogen sulfide). However, in contrast to what has been observed in similar conversions of furan and its homologs [6], it appears that in the oxazole series the replacement of bridge oxygen by other heteroatoms proceeds with greater completeness the lower the acidity of the reagent employed.

On this rule depends the possibility of obtaining the imidazoles in high yields (up to 70%) [3], the N-arylimidazoles in lesser yields (up to 50%) [2], and the thiazoles in small yields from the oxazoles.

We were not able to accomplish the catalytic conversion of 2-methylbenzoxazole to 2-methylbenzothiazole: 50% of unchanged 2-methylbenzoxazole was recovered from the reaction, while the remaining portion of it underwent decomposition. In this connection it should be noted that Theilig [4] did not obtain 2-methylbenzimidazole by the action of formamide on 2-methylbenzoxazole, while the alkyloxazoles upon reaction with this reagent gave good yields of the corresponding alkylimidazoles.

Inasmuch as the catalytic conversion studied by us of the isomeric dimethyloxazoles, and also the trimethyloxazole, to the respective thiazoles proceeded with almost identical yields, it is apparent that because of the presence of a tertiary nitrogen atom in the ring this reaction has little dependence on the position and number of the methyl groups or on the temperature within the range 300-375°.

As is well known, in the furan series the position of the methyl groups in the ring and their number have a substantial effect on the yield of the corresponding thiophenes.

EXPERIMENTAL

Alkyloxazoles and their constants. 2,5-Dimethyloxazole was obtained in the amount of 30 g by the method of Treibs [7]:

b. p. 115-117° (760 mm), n_D^{21} 1.4394, d_4^{21} 0.9856, MR_D 25.97. $C_5H_7ONF_2$. Calculated: 27.74; EM_D — 1.79.

Literature data [8]: b. p. 116-117°, n_D^{25} 1.4365; [9]: n_{He}^{20} 1.439, d_4^{20} 0.997, EM_D — 1.72.

4,5-Dimethyloxazole was obtained in the amount of 100 g by the method of Bredereck and Theilig (II):

b. p. 115-117° (755 mm), n_D^{20} 1.4432, d_4^{20} 0.9966, MR_D 25.82. $C_5H_7ONF_2$. Calculated: 27.74; EM_D — EM_D — 1.92.

Found %: N 14.28. C_5H_7ON. Calculated %: N 14.42.

In the work of Bredereck and Theilig [11] an incorrect boiling point (129-135° at 760 mm) for 4,5-dimethyloxazole was mistakenly given without indicating the other constants.

4,5-Dimethyloxazole methiodide. 0.9 g of 4,5-dimethyloxazole and 1.4 g of methyl iodide were heated for 1 hour at 100°: m. p. 137° (from anhydrous alcohol with precipitation by ether).

Found %: N 5.86, 5.80. $C_6H_{10}ONI$. Calculated %: N 5.85.

2,4-Dimethyloxazole was prepared by the method of Theilig [4] in the amount of 40 g:

b. p. 106-108° (750 mm), n_D^{20} 1.4389, d_4^{20} 0.9757, MR_D 26.18. $C_5H_7ONF_2$. Calculated: 27.86; EM_D — 1.56.

Methiodide: m. p. 247°.

Literature data [4]: b. p. 103-110° (760 mm); [12]: b. p. 97-107°. Methiodide: decomp. temp. 235°; [9]: b. p. 95°, n_{He}^{20} 1.414, d_4^{20} 0.931; EM_D − 1.24.

2,4,5-Trimethyloxazole was prepared by the method of Bredereck and Theilig [11] in the amount of 30 g:

B. p. 137-138° (760 mm), n_D^{20} 1.4425, d_4^{20} 0.9569, MR_D 30.76. $C_6H_9ONF_2$. Calculated: 32.36; EM_D −1.60. Picrate: m. p. 113° (from anhydrous alcohol). Adduct with $HgCl_2$: m. p. 166° (from anhydrous alcohol).

Literature data [13]: b. p. 132-133°, n_D^{25} 1.4412, d_{15}^{25} 0.9566; [7]: b. p. 135° (720 mm). Adduct with $HgCl_2$: m. p. 165°; [10]: Picrate with m. p. 115°.

Conversion of alkyloxazoles to alkylthiazoles. 2,5-Dimethylthiazole. Nine g of 2,5-dimethyloxazole was passed over aluminum oxide at 350° at the rate of 0.3 ml/min. in a current of hydrogen sulfide. The catalyzates obtained in three experiments were saturated with potassium carbonate and extracted with ether. After the ether was distilled off from the ether extract, which had been dried with anhydrous potassium carbonate, the residue was fractionated, yielding 3.6 g (13% of the amount introduced into the reaction) of unchanged 2,5-dimethyloxazole (b. p. 115-117°, n_D^{20} 1.4390) and 3.6 g of 2,5-dimethylthiazole, which had the following constants:

b. p. 151-153° (760 mm), n_D^{20} 1.4898, d_4^{20} 1.0280, MR_D 32.76. $C_5H_7NSF_2$. Calculated: 33.49; EM_D − 1.73.

Yield 13% of theoretical, calculated on the basis of the 2,5-dimethyloxazole used.

Found %: N 12.17. C_5H_7NS. Calculated %: N 12.39.

Picrate: m. p. 172° (from anhydrous alcohol).

Literature data [14]: b. p. 148.9°-150.9° (743 mm), 153° (758 mm); [9]: b. p. 153° n_{He}^{20} 1.511, d_4^{20} 1.058.

At 300° the yield of 2,5-dimethylthiazole (calculated on the basis of the 2,5-dimethyloxazole) was 13%, at 375° − 12%.

4,5-Dimethylthiazole. From three experiments using 8.9 g of 4,5-dimethyloxazole each, which was passed over aluminum oxide at 375° at a rate of 0.4 ml/min. in a current of hydrogen sulfide, there was obtained, after appropriate treatment of the reaction product, by distilling off 2.7 g (10%) of unchanged 4.5-dimethyloxazole (b. p. 115-117°), and by fractionating in vacuo, 4.5 g of 4,5-dimethylthiazole that had the following constants:

b. p. 75-77° (47 mm), n_D^{20} 1.5193, d_4^{20} 1.0699. MR_D 32.12. $C_5H_7NSF_2$. Calculated: 33.49; EM_D − 1.37.

Yield 15.5% of theoretical calculated on the basis of the 4,5-dimethyloxazole used.

Picrate: m. p. 187° (from anhydrous alcohol).

Found %: N 16.21, 16.36. $C_{11}H_{10}O_7N_4S$. Calculated %: N 16.36.

Literature data [15]: b. p. 75° (47 mm).

2,4-Dimethylthiazole. From three experiments using 6.9 g of 2,4-dimethyloxazole each, which was passed over aluminum oxide at 375° at a rate of 0.5 ml/min. in a current of hydrogen sulfide, there was obtained, after appropriate treatment of the catalyzate, by distillation of the reaction product, 2.4 g (12%) of unchanged 2,4-dimethyloxazole (b. p. 106-108°, n_D^{20} 1.4390) and 2.4 g of 2,4-dimethylthiazole that had the following constants:

b. p. 67-68° (50 mm), n_D^{20} 1.5095, d_4^{20} 1.0513, MR_D 32.17. $C_5H_7NSF_2$. Calculated: 33.49; EM_D − 1.32.

Yield 12.0% calculated on the basis of the 2,4-dimethyloxazole used.

Picrate: m. p. 137-138° (from anhydrous alcohol).

Found %: N 16.72, 16.74. $C_{11}H_{10}O_7N_4S$. Calculated %: N 16.36.

Literature data [16]: b. p. 142.5-143°, d^{15} 1.0601, picrate with m. p. 137-138°; [15]: b. p. 70-71° (50 mm); [9]: b. p. 143°, n_{He}^{20} 1.509, d_4^{20} 1.057; [18]: picrate with m. p. 135°.

2,4,5-Trimethylthiazole. From three experiments using 6.9 g of 2,4,5-trimethyloxazole each, which was passed over aluminum oxide at 375° at a rate of 0.5 ml/min. in a current of hydrogen sulfide, there was obtained, after the usual treatment of the reaction product and distillation, 3.2 g (12%) of unchanged 2,4,5-trimethyloxazole (b. p. 137-139°) and 2.4 g of 2,4,5-trimethylthiazole that had the following constants:

b. p. 64-66° (20 mm), n_D^{20} 1.5023, d_4^{20} 1.0327, MR_D 36.37. C_6H_9NS. Calculated: 38.11; EM_D – 1.74.

Yield 10% of theoretical calculated on the basis of the 2,4,5-trimethyloxazole used.

Found %: N 11.37, 11.32. C_6H_9NS. Calculated %: N 11.00.

Picrate: m. p. 132° (from anhydrous alcohol).

Literature data [17]: b. p. 165-166° (717.5 mm), d^{16} 1.0130, picrate with m. p. 133°; [15]: b. p. 65-67° (20 mm).

SUMMARY

The isomeric dimethyloxazoles (2,4-, 2,5-, and 4,5-) and 2,4,5-trimethyloxazole, when acted upon by hydrogen sulfide in contact with aluminum oxide at an elevated temperature undergo, like other five- and six-membered oxygen-containing heterocycles, replacement of bridge oxygen by sulfur with the formation of the corresponding dimethylthiazoles (2,4-, 2,5-, and 4,5-,) and 2,4,5-trimethylthiazole.

Because of the presence of a tertiary nitrogen atom in the oxazole ring the yield of the isomeric dimethylthiazoles prepared catalytically by the conversion of the corresponding oxazoles has little dependence on the position of the methyl groups in the ring of the latter.

Catalytic conversion of the oxazole ring to the thiazole ring proceeds according to the same reaction mechanism as that established for the analogous conversion of furan to thiophene, but the oxazole ring shows considerably greater stability than that of furan toward the action of an reagent of acid character– hydrogen sulfide– under these conditions.

LITERATURE CITED

[1] Iu. K. Iur'ev, J. Gen. Chem. 6, 972, 1669 (1936); Scientific Report, Moscow State Univ. 79 (1945). (Monograph).

[2] M. Lewy, Ber. 21, 2192 (1888); S. Minovici, Ber. 29, 2097 (1896).

[3] J. Cornforth and R. Cornforth, J. Chem. Soc. 1947, 96; J. Cornforth and H. Huang, J. Chem. Soc. 1948, 1960.

[4] G. Theilig, Ber. 86, 96 (1953).

[5] Z. Fôldi, Acta Chim. Acad. Sci. Hungaricae, 3, 501 (1953).

[6] Iu. K. Iur'ev and I. K. Korobitsyna, J. Gen. Chem. 21, 973 (1951);* Iu. K. Iur'ev, I. K. Korobitsyna and M. Ia. Kuznetsova, J. Gen. Chem. 20, 1493 (1950).*

[7] A. Treibs and M. Sutter, Ver. 84, 96 (1951).

[8] R. Wiley and O. Borum, J. Am. Chem. Soc. 70, 2005 (1948).

[9] K. Auwers and Ernst, Z. phys. Ch. 122, 217 (1926).

[10] A. Wrede and G. Feuerrigel, Z. physiol. Ch. 218, 129 (1933).

[11] H. Bredereck and G. Theilig, Ber. 86, 88 (1953).

[12] Ch. Zinsstag and B. Prijs, Helv. Chim. Acta, 32, 148 (1949).

[13] R. Wiley, J. Org. Ch. 12, 43 (1947).

*Original Russian pagination. See C. B. Translation.

[14] S. Gabriel, Ber. 43, 134, 1286 (1888).

[15] R. Kurkju and E. Brown, J. Am. Chem. Soc. 74, 5778 (1952).

[16] A. Hantzsch, Lieb. Ann. 250, 266 (1889).

[17] T. Rubleff, Lieb. Ann. 259, 258 (1890).

[18] M. Stende, Lieb. Ann. 261, 41 (1891).

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RADICAL AND ION ALKYLATION OF THE AROMATIC RING

VI. REACTIONS OF DIPHENYLCHLOROMETHANE WITH TOLUENE AND BENZENE

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Little work has been devoted to the use of diphenylchloromethane in alkylation reactions. Boeseken [1] studied this reaction with benzene in the presence of $AlCl_3$ and showed that the normal product, triphenylmethane, was formed in insignificant yield and the chief products were diphenylmethane (35%) and triphenylchloromethane (30%). Pfeiffer [2] pointed out the formation of triphenylmethane in the reaction of diphenylbromomethane with benzene in the presence of $SnCl_4$. Thermal (and catalytic with $ZnCl_2$) alkylation of phenols with diphenylchloromethane was accomplished by Alphen [3], and with diphenylbromomethane by Busch [4]. On heating diphenylbromomethane and pyridine in sealed tubes Chichibabin [5] isolated a negligible amount of benzohydrylpyridine along with tetraphenylethylene (50%) and diphenylmethane (20%).

Continuing an investigation of the use of a copper catalyst for alkylation [6, 7] we undertook a study of reactions with diphenylchloromethane. In a previous article [6] it was reported that thermal and catalytic benzylation of a number of aromatic compounds was accomplished, and on the basis of the data obtained it was assumed that the reaction proceeds with homolytic redistribution of the bonds in the reaction complex without the formation of free radicals.

The choice of diphenylchloromethane as the object of the present work was explained, on the one hand, by the insufficient investigation of alkylation reactions with benzohydryl halides, and on the other hand, by the striving to obtain complete information on the mechanism of these reactions. There was an indication [8] that diphenylchloromethane on treatment with metallic silver forms free radicals: in the absence of air tetraphenylethane was formed in quantitative yield; in oxygen the principle products were various oxygen-containing compounds along with a small amount of tetraphenylethane (2-8%). Under the reaction conditions studied we also might expect the appearance of free radicals under the influence of the copper on the diphenylchloromethane and in connection with this a change in the course of the synthesis of benzohydryl-substituted aromatic compounds.

We have shown that the reaction of diphenylchloromethane with toluene in the presence of small amounts of copper (0.1 g-equiv.) at 115-140° proceeds with the formation of p-benzohydryltoluene (54%) as the main product; the o-isomer and tetraphenylethane are formed as negligible contaminants. In some reactions diphenylmethane also was found. Carrying out the reaction in a current of nitrogen or of oxygen did not change the course of the process.

We were not able to accomplish the introduction of the benzohydryl group into the benzene molecule under analogous conditions. Triphenylmethane was obtained in negligible yield at 200°. Heating equimolecular amounts of copper and diphenylchloromethane in benzene solution yielded tetraphenylethane (67.5%); triphenylmethane was formed in very trifling amount in some reactions. Carrying out the reaction in oxygen gave the same results. It was established that CuCl and HCl, as in the benzylation reactions also, are not catalysts.

The data presented show that the transition from benzyl chloride to diphenylchloromethane does not result in a change in the reaction mechanism: neither in the alkylation nor in the dimerization reaction (synthesis of tetraphenylethane in benzene solution) do free radicals appear. Otherwise the formation of oxygen-containing products must be expected on carrying out the reaction in oxygen [8]. This conclusion also is

confirmed by the thermal reactions with diphenylchloromethane, which proceed differently than thermal benzylation reactions. It is known that distillation of diphenylchloromethane at atmospheric pressure is accompanied by decomposition. Engler [9] obtained tetraphenylethylene and HCl in this way. Anschütz [10], when he reproduced these experiments, noted the formation of tetraphenylethane and HCl (the products were not fully investigated).

We have shown that thermal decomposition of diphenylchloromethane at 300-305° leads to the formation of tetraphenylethylene (89%) and HCl. In benzene also tetraphenylethylene (92%) and HCl are formed. In toluene and cyclohexane the yield of tetraphenylethylene decreases (47 and 56% respectively); besides this, a nearly equivalent amount of diphenylmethane is formed (40 and 38.5%). The decomposition reaction in toluene, which is not deep-seated, yields tetraphenylethylene and tetraphenylethane. To explain the formation of these products it may be assumed that in the first stage the dissociation of diphenylchloromethane to a diphenylmethyl radical and an atom of chlorine (I) occurs. The diphenylmethyl radical then may undergo dimerization (II) and disproportionation (III):

$$(C_6H_5)_2CHCl \rightarrow (C_6H_5)_2CH\cdot + Cl. \qquad (I)$$

$$2(C_6H_5)_2CH\cdot \rightarrow (C_6H_5)_2CHCH(C_6H_5)_2 \qquad (II)$$

$$4(C_6H_5)_2CH\cdot \rightarrow 2(C_6H_5)_2CH_2 + (C_6H_5)_2CH{=}CH(C_6H_5)_2 \qquad (III)$$

At 300° the disproportionation (III) dominates. In the absence of a solvent (and in benzene) the chlorine atom dehydrogenates the diphenylmethane to the diphenylmethyl radical, which then undergoes a similar conversion, so that the final product is tetraphenylethylene. In solvents that have more active hydrogens the solvent undergoes dehydrogenation (the C—H bond in diphenylmethane is weaker, but the solvent is present in great excess).

The fact that tetraphenylethylene is not formed through a stage of tetraphenylethane was shown by experiments on the decomposition of diphenylchloromethane in it. The reaction proceeded with much tar formation, and diphenylmethane was isolated (42%) with only a trifling admixture of tetraphenylethylene.

The decomposition of diphenylchloromethane in the presence of diphenylmethane led, as might be expected on the basis of the assumed mechanism, to the formation of tetraphenylethylene (86.4%) while the amount of diphenylmethane remained unchanged.

In other cases products of the conversion of radicals through the solvent have not been discovered up to the present time. The possibility of decomposition of diphenylchloromethane with the formation of a diphenylmethylene biradical also should be taken into account.

Summing up what has been stated above, we arrive at the conclusion that the mechanism of the catalytic reactions described in the presence of copper is similar to the mechanism of benzylation: the reactions proceed with homolytic redistribution of the bonds within the reaction complex, in the formation of which the catalyst takes part. In thermal reactions of diphenylchloromethane, in contrast to such reactions of benzyl chloride, free radicals play a part.

EXPERIMENTAL

Reactions of diphenylchloromethane with toluene were carried out in a flask with a reflux condenser connected through a calcium chloride tube with an absorbing bottle. The diphenylchloromethane and then the toluene were added to the copper, and the mixture was heated on a sand bath for 3-7 hours at 112-140° (thermometer in the liquid) until the evolution of HCl almost completely ceased. At the end of the reaction the mixture was filtered off from the inorganic residue and the latter was treated several times with hot toluene. The toluene used for washing was combined with the filtrate which, after the solvent was distilled off, was fractionated in vacuo. The p-benzohydryltoluene fraction was always obtained as an oil, which crystallized only upon prolonged standing. But addition to the oil of a small amount of methyl or ethyl alcohol or ether caused rapid crystallization as a result of transition to a solution of the o-isomer. The melting point of the p-isomer was 70-71° (literature data: 69-70° [11]). From methyl alcohol (which was usually used) the o-isomer separated on long standing, m. p. 80-82° (literature data 80-83° [12]).

The tetraphenylethane was pressed out on a porous plate and recrystallized from benzene. M. p. 208-210°. A mixed melting point test with a known sample gave no depression. Diphenylmethane, which was obtained in several reactions, was demonstrated by the preparation of the 4,4'-dinitro derivative with m. p. 181-185° [13] (Table 1).

TABLE 1

Reactions of Diphenylchloromethane with Toluene

Molecular ratio $(C_6H_5)_2CHCl : Cu : C_7H_8$	Reaction conditions			Yield of reaction products (%)	
	temperature	time (hours)	medium	p-benzohydryltoluene	tetraphenylethane
1 : 0.1 : 3	96°	12	Air	9.6	—
1 : 0.1 : 10	111—113	7.5	Nitrogen	16.9	5.9
1 : 0.1 : 3	115—138	7.5	Air	54	5.9
1 : 1 : 3	112—140	2.5	Nitrogen	41.5	30.8
1 : 0.09: 2.7	118—197	5	Nitrogen	38.4	2.8
1 : 0.1 : 3	112—140	7	Oxygen	44.5	3.5

Reactions of diphenylchloromethane with benzene at 84-120° were carried out similarly to the experiments with toluene. The method of workup of the mixture, when large amounts of tetraphenylethane were formed, was different: after the reaction was completed, a 5-10 times excess of benzene was added and the hot mixture was filtered off from the inorganic residue. Most of the solvent was removed by distillation, and from the small residue the tetraphenylethane crystallized. M. p. 207-208°. The mother liquor was distilled in vacuo.

Triphenylmethane usually was mixed with tetraphenylethane and decomposition products. It was separated from tetraphenylethane by washing 2-3 times with alcohol. The crystals obtained upon evaporation of the alcohol were purified by recrystallization from benzene. M. p. 91-93°; a mixed sample with a known preparation melted at 91-93° (Table 2).

TABLE 2

Reactions of Diphenylchloromethane with Benzene

Molecular ratio $(C_6H_5)_2CHCl : Cu : C_6H_6$	Reaction conditions		Reaction products (%)	
	temperature	time (hours)	tetraphenylethane	triphenylmethane
1 : 0.1 : 3	87—92°	13	2.8	—
1 : 0.1 : 3 *	150	7.5	2.8	—
1 : 0.12 : 3 *	200	7.5	3	4
1 : 1 : 5.2	85—86	7.5	51	2.4
1 : 1 : 2	86—120	3	64	—
1 : 1 : 5.2 **	84—100	6	67.5	2.4
1 : 1 : 5 ***	85— 86	7	55	—

*Experiments were carried out in an autoclave.

**Benzene was introduced in two portions with an interval of 1.5 hours.

***Experiment in a current of oxygen.

TABLE 3

Decomposition of Diphenylchloromethane by Heating to 300-305° in the Course of 7-7.5 Hours

Amount of diphenyl-chloro-methane (g)	Solvent and amount (g)	Yields of reaction products				
		tetraphenylethylene		diphenylmethane		tar
		g	(%)	g	(%)	
5.1		3.7	89	—	—	0.5
5.1	Benzene (6.2)	3.85	92.3	—	—	0.3
5.1	Toluene (6.2)	1.95	46.8	1.7	40	1
5.1	Cyclohexane (6.35)	2.35	56.5	1.6	38.5	0.2
5.1	Tetraphenylethane (3)	0.05	1.2	1.8	42.5	2.45
2.55	Diphenylmethane (1)	1.8		1		0.2

Thermal decomposition of diphenylchloromethane. The reactions were carried out in sealed ampoules, which were heated in an autoclave to 300-305° in the course of 7-7.5 hours. When low-boiling solvents were used, the appropriate solvent was poured into the autoclave. Before closing the ampoule in some instances (decomposition in diphenylmethane) thorough cooling was required (solid carbon dioxide). The contents of the ampoule were carefully extracted with a suitable solvent or benzene. The crystals that separated from the cooled solution were removed and the mother liquor was fractionated (Table 3).

SUMMARY

1. Reactions of diphenylchloromethane with toluene and benzene in the presence of copper have been studied. With toluene (0.1 g-equiv. of copper) p-benzohydryltoluene was obtained (54%); with benzene (equimolecular amount of copper) the main product was tetraphenylethane (68%).

New experimental data are adduced which confirm the opinion expressed previously that free radicals are not formed under the conditions considered.

2. Thermal decomposition reactions of diphenylchloromethane have been studied in a number of aromatic compounds and in cyclohexane; a free-radical mechanism has been proved for them.

LITERATURE CITED

[1] J. Boeseken, Zbl. 1903, II, 202.

[2] P. Pfeiffer, Eistert, J. pr. Ch. [2], 124, 183 (1930).

[3] J. Alphen, Rec. trav. chim. 46, 799 (1927).

[4] M. Busch and R. Knoll, Ber. 60, 2243 (1927).

[5] A. E. Chichibabin, J. Russ. Phys. Chem. Soc. 34, 135 (1902).

[6] I. P. Tsukervanik and S. G. Mel'kanovitskaia, J. Gen. Chem. 27, 885 (1957).*

[7] I. P. Tsukervanik and G. S. Semeshko, J. Gen. Chem. 27, 1133 (1957).*

[8] W. Th. Nauta and D. Mulder, Ch. A. 34, 1985 (1940).

[9] C. Engler and H. Bethge, Ber. 7, 1128 (1874).

[10] R. Anschütz, Lieb. Ann. 235, 220 (1886).

[11] Beilst., V, 710.

*Original Russian pagination. See C. B. Translation.

[12] Beilst., V, 709.

[13] Beilst., V, 595.

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CHLORINATION OF FIVE- AND SIX-MEMBERED CYCLANES*

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The investigation of chlorination processes of the cycloparaffins has repeatedly attracted the attention of many investigators who have sought to find ways of going from the chemically inert cycloparaffins to the reactive halogen derivatives.

The halogenation reactions of cyclanes and alkanes are in many respects similar to each other, but they also have some differences.

The literature on the chlorination of cyclanes contains a limited amount of experimental data. Many studies on the halogenation of five- and six-membered cyclic hydrocarbons have been carried out with petroleum fractions; the conditions of halogenation are not fully enough indicated.

To the early studies in this field belong the classic investigations of V. V. Markovnikov [1], who prepared monochlorocyclohexane with b. p. 142° (750 mm) by the action on cyclohexane of moist chlorine in the cold and with irradiation by sunlight. When dry chlorine was used, Markovnikov heated the hydrocarbon almost to its boiling point. This process led to the formation also of polychloro derivatives. By distillation of the chlorination products of cyclohexane Markovnikov separated two isomeric dichlorocyclohexanes.

A careful investigation was carried out by E. Fortey [2], who conducted a photochemically catalyzed chlorination of cyclohexane. The hydrocarbon was placed together with a small amount of iron filings in an apparatus equipped with a reflux condenser, and a current of dry chlorine was passed through it in the direct sunlight at room temperature for several hours. A mixture of di- and polychloroderivatives was obtained on fractional distillation of the chlorination products; the monochloro derivative was not formed. Fortey also carried out the chlorination of cyclohexane with dry chlorine in the cold with irradiation by daylight for 3 hours. In this case he isolated monochlorocyclohexane and two isomeric dichlorocyclohexanes by fractional distillation of the reaction product.

N. D. Zelinskii [3] carried out the vapor-phase chlorination of cyclohexane in a specially constructed apparatus which met the following conditions: "1) The monochloride was immediately taken out of the sphere of the reaction, 2) only the low-boiling fractions of the mixture were continuously admitted to the sphere of reaction, 3) the chlorine introduced into the reaction was in excess of the hydrocarbon vapors." By chlorination in the light for 27.5 hours N. D. Zelinskii obtained a product with a yield, calculated as monochloride, of 90%. By photochemical chlorination of cyclohexane in a Zelinskii chlorinator, N. I. Shuikin [4] obtained chlorocyclohexane in 38.4% yield calculated on the starting hydrocarbon; the yield based on reacted cyclohexane was 83.4%.

A more complete study of the halogenation reactions of the simplest cyclopentane and cyclohexane hydrocarbons might not only be of considerable interest, but also reveal a way for the utilization of these hydrocarbons, for example, for the preparation of cyclic secondary alcohols and other derivatives. Recently the halogen derivatives of the cyclanes have found wide use in agriculture as insecticides.

EXPERIMENTAL

The starting cyclanes had the following properties: cyclopentane—b. p. 49-49.5° (755 mm), d_4^{20} 0.7455, n_D^{20} 1.4063; cyclohexane—b. p. 80.5-81° (752 mm), d_4^{20} 0.7788, n_D^{20} 1.4263.

*L. N. Karchenko participated in conducting the experiments.

The constants found were close to the data in the literature [5].

For convenience in comparing the results obtained by chlorination by different methods, a single procedure was adopted in the present work for working up the chlorination products: they were carefully washed with sodium carbonate and with water, were dried with calcium chloride, and then subjected to fractional distillation in vacuo on a column with an efficiency of 40 theoretical plates. On the basis of the data on the boiling limits of the individual fractions and other of their physicochemical properties the content of mono-, di- and polychlorides was determined in the chlorination products. As characteristics of the chloro products their constants and their chlorine content were determined.

TABLE 1

Physicochemical Properties of Individual Chloro Derivatives

Chlorocyclane fractions	Boiling temperatures (pressure in mm)	d_4^{20}	n_D^{20}	MR_D		Chlorine content (%)	
				found	calc.	found	calc.
Monochlorocyclopentane fraction	114—115 (752)	1.0050 – 1.0052	1.4500 – 1.4512	27.81 – 28.3	27.96	33.0, 33.5	33.3
Dichlorocyclopentane fraction	79.5—81.0 (50)	1.1759 – 1.1792	1.4682 – 1.4686	32.76 – 32.86	32.82	50.25, 50.35	50.31
Monochlorocyclohexane fraction	140—142 (752)	0.9990 – 0.9993	1.4623 – 1.4625	32.44 – 32.55	32.58	29.00, 29.15	29.08
Dichlorocyclohexane fraction	105.5—115.0 (50)	1.1670 – 1.1704	1.4811 – 1.4814	37.02 – 37.22	37.44	46.30, 46.43	46.37

On the basis of the first rough experiments on the separation of the chlorination products of cyclopentane and cyclohexane it was recognized as expeditious, for convenience in carrying out serial analyses, to take fractions for the monochlorocyclanes, dichlorocyclanes, and polychlorocyclanes having the properties given in Table 1, corresponding to the literature data [2].

The first group of experiments (1-22) — the thermal chlorination of cyclopentane and cyclohexane — was carried out in a catalytic tube filled with inert material (glass beads), heated by an electric furnace with an automatic regulator. Experiments were set up with moist and dry chlorine. In this way the optimum temperature and ratio of hydrocarbon to chlorine were shown. The results of the experiments are given in Table 2.

From the data given in Table 2 it follows that a change in the temperature of chlorination within the limits from 250 to 270° (with other conditions constant) does not have an appreciable effect on the yield of monochlorocyclopentane. The presence of traces of moisture in the reaction field has a substantial effect on the character of the chlorination of cyclopentane. In case of the use of dry chlorine the yield of polychlorides is somewhat increased and the formation of monochloropentane is decreased. In experiments with moist chlorine, however, the yield of the monochloride is increased, with a decrease in the formation of polychlorides.

A study of the chlorination of cyclohexane showed (Table 3) that the optimum temperature for this process under the conditions used was 320-340°. Here also the presence of moisture in the reaction field had substantial significance. The use of moist chlorine led to an increase in the yield of monochloride and a decrease in the formation of polychlorides.

The second group of experiments (54-71) was devoted to a study of the photochemical chlorination of cyclanes in the vapor phase in the apparatus of N. D. Zelenskii [3] in daylight. The initial temperature of the reaction mixture in the upper globe of the chlorinator was 30-35°; the temperature of the experiment was further maintained within the limits 40-45°. The results of the experiments are given in Tables 4 and 5, from

TABLE 2

Thermal Chlorination of Cyclopentane. Duration of Experiments 180 Minutes, 17.5 g Cyclopentane and 7.6 l Chlorine Used (molar ratio cyclopentane : chlorine = 1 : 1.4)

Expt. No.	Temperature	Yield of condensate (g)	Composition of condensate (%)			
			unreacted cyclopentane	monochloride	dichlorides	polychlorides
			Dry chlorine			
5	250°	22.5	10.8	36.9	34.3	18.0
10	260	22.4	3.8	37.8	37.5	18.9
14	270	22.4	—	39.3	41.7	19.0
			Moist chlorine			
16	250	22.6	10.2	41.4	35.0	13.4
19	260	22.5	2.7	43.0	38.0	15.3
22	270	22.5	—	45.3	39.0	15.7

TABLE 3

Thermal Chlorination of Cyclohexane. Duration of Experiments 180 Minutes; in Each Experiment 14 g of Cyclohexane and 5.0 l of Chlorine were Used

Expt. No.	Temperature	Yield of condensate (g)	Composition of condensate (%)			
			unreacted cyclohexane	monochloride	dichlorides	polychlorides
			Dry chlorine			
23	280°	19.4	27.7	36.3	36.0	—
27	290	19.4	26.8	37.5	35.7	—
31	300	19.4	21.3	39.0	37.3	2.4
35	320	19.4	12.5	39.7	38.5	9.3
39	330	19.4	3.7	41.3	42.5	12.5
42	340	19.4	—	41.9	43.8	14.3
			Moist chlorine			
45	320	19.5	11.5	43.9	39.0	5.6
49	330	19.4	3.3	46.0	40.3	10.4
53	340	19.4	—	48.3	41.0	10.7

the data of which it is seen that, as in the case of thermal chlorination also, the best yield of monochlorides was obtained when moist chlorine was used. But carrying out the reaction with dry chlorine, markedly increased the content of more highly chlorinated cyclanes in the reaction products.

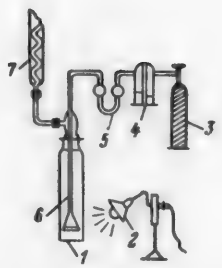
The third group of experiments (72-99) – photochemical chlorination of cyclanes in the liquid phase – was carried out by our using chlorine admitted to the reaction in the apparatus shown schematically in the figure.

The hydrocarbon was placed in the cylindrical reactor (1), illuminated at a distance of 18 cm by an electric lamp (2) with a power of 200 w. Chlorine from the cylinder (3) passed through the Tishchenko bottle (4) with concentrated sulfuric acid and was introduced through the rheometer (5) into the hydrocarbon at room temperature (15-17°) through the capillary tubules (6) which were lowered to the bottom of the reactor. The gaseous reaction products escaped from the reactor into the condenser (7). The hydrocarbon vapors were condensed to a liquid, which ran back into the reactor.

TABLE 4

Photochemical Chlorination of Cyclopentane in the Vapor Phase. Duration of Experiments 4.5 Hours; in Each Experiment 35 g of Cyclopentane and 11 l of Chlorine were Used (molar ratio 1 : 1)

Expt. No.	Yield of condensate (g)	Composition of condensate (%)			
		unreacted cyclopentane	monochloride	dichlorides	polychlorides
		Dry chlorine			
54	40.3	10.4	34.5	35.3	22.8
57	40.5	10.7	32.7	34.9	21.7
		Moist chlorine			
59	40.4	10.0	39.7	32.5	17.0
61	40.6	10.6	40.0	32.1	16.6



Scheme of apparatus for the photochemical chlorinization of hydrocarbon. (Explanation in text).

The hydrogen chloride passed through the condenser into a absorbing apparatus, where it was collected in water.

Because of a shortage of cyclopentane its chlorination was not fully investigated, but even those few experiments that were carried out with it showed that with a molar ratio of cyclopentane and chlorine of 1 : 1.5 and an experiment time of 5.5 hours the condensate contained 60.4% monochlorocyclopentane, 24.5% dichlorides, and 15% polychlorides. The results of the experiments with cyclohexane are given in Table 6.

From the data of this Table it is evident that with an increase in the ratio of cyclohexane to chlorine from 1 : 1 to 1 : 6.5 the formation of polychlorides was notably increased and the formation of monochlorides decreased.

TABLE 5

Photochemical Chlorination of Cyclohexane in the Vapor Phase. Duration of Experiments 4.5 Hours; in Each Experiment 42 g of Cyclohexane and 10.9 l of Chlorine (molar ratio 1 : 1) were used

Expt. No.	Yield of condensate (g)	Composition of condensate (%)			
		unreacted cyclohexane	monochloride	dichlorides	polychlorides
		Dry chlorine			
63	47.0	10.6	33.8	35.6	20.0
65	47.3	10.4	31.0	35.3	20.3
		Moist chlorine			
68	46.9	10.4	40.7	31.9	17.0
71	47.2	10.3	41.0	32.3	16.4

TABLE 6

Photochemical Chlorination of Cyclohexane in the Liquid Phase

Expt. No.	Duration of experiments (hrs)	Used		Moles cyclohexane : chlorine	Yield of condensate (g)	Composition of condensate (%)			
		cyclohexane (g)	chlorine (liters)			monochloride	dichlorides	trichlorides	polychlorides
				Dry chlorine					
85	19.0	14.0	12.3	1:3.5	26.0	16.0	23.0	21.5	39.2
89	16.0	14.0	16.2	1:4.5	26.6	—	29.3	23.3	47.3
93	19.4	14.0	23.4	1:6.5	33.7	—	9.8	20.9	69.2
				Moist chlorine					
97	13.0	14.0	12.2	1:3.5	26.0	20.2	23.0	26.3	30.5
99	19.4	14.0	23.4	1:6.5	34.0	—	19.0	30.7	50.3

As also in the other methods of chlorination, here the use of moist chlorine led to some increase in the yield of monochlorides.

SUMMARY

1. The thermal and photochemical chlorination with dry and moist chlorine of cyclopentane and cyclohexane in the liquid and vapor phases has been studied.

2. The conditions have been found that permit obtaining, as desired, principally mono- or polychlorinated products.

3. The advantages of liquid-phase chlorination of five- and six-membered cyclanes have been demonstrated.

LITERATURE CITED

[1] W. Markovnikov; Lieb. Ann. 302, 1 (1898).

[2] E. C. Fortey, J. Chem. Soc. 73, 932 (1898).

[3] N. D. Zelinskii and B. V. Maksorov, J. Chem. Indus. 1, 5 (1924).

[4] N. I. Shuikin, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1944, 442.

[5] R. D. Obolentsev, Physical Constants of the Hydrocarbons of Liquid Fuels and Oils*, Gostoptekhizdat (1953).

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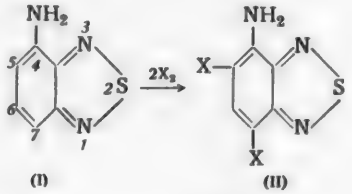
STUDIES IN THE FIELD OF THE CHEMISTRY OF 2,1,3-THIODIAZOLE

VI. CHLORINATION AND BROMINATION OF 4- AND 5-AMINOBENZO-2,1,3-THIODIAZOLES

V. G. Pesin and A. M. Khaletskii

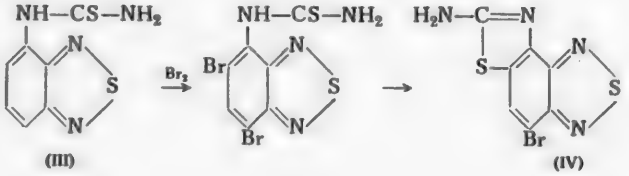
We have shown previously [1] that 4- and 5-aminobenzo-2,1,3-thiodiazoles are easily acylated under the usual conditions for aromatic amines. In the present communication data are presented on an investigation of chlorination and bromination reactions of 4- and 5-aminobenzo-2,1,3-thiodiazoles.

The high reactivity characteristic of aniline is fully observed in 4-aminobenzo-2,1,3-thiodiazole (I). Thus, upon chlorination and bromination of the latter the main products are the 4-amino-5,7-dihalobenzo-2,1,3-thiodiazoles (II). When equimolecular amounts of the reactants are used for the reaction, part of the 4-aminobenzo-2,1,3-thiodiazole does not enter into the reaction, and the corresponding disubstituted compounds are formed in approximately 40-45% yield. When the conduct of the reaction is based on an estimation of the production of dihalogen derivatives (where X is chlorine or bromine), the latter are formed in high yields.



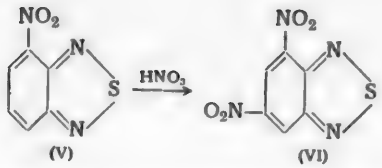
(I) (II)

A high reactivity also is noted for acylated 4-aminobenzo-2,1,3-thiodiazole. Thus, for example, when benzo-2,1,3-thiodiazole-4-thiourea (III) is brominated, mainly the dibromo derivative is formed, which is converted to the corresponding derivative of benzothiodiazole (IV).



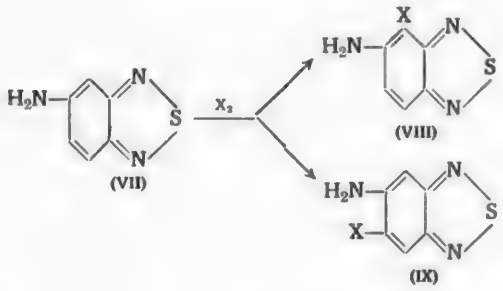
(III) (IV)

These data show that the direction of substitution in the hydrocarbon ring is determined by the amino group, since no effect at all of the thiodiazole ring appears. The same fact is noted in the literature [2] for nitration of 4-nitrobenzo-2,1,3-thiodiazole (V); the second nitro group enters position 6, i.e., substitution occurs under the influence of the nitro group already present (VI) (the effect of the thiodiazole ring does not make itself felt).



(V) (VI)

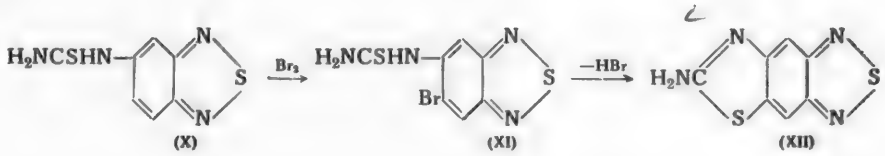
Thus, on chlorination and bromination of 4-aminobenzo-2,1,3-thiodiazole (VII) the latter behaves like a typical aromatic primary amine. This predominant effect of substituent in the hydrocarbon ring on the place of entrance of another substituent is observed in still greater degree in the chlorination or bromination of 5-aminobenzo-2,1,3-thiodiazole. In this case the halogen can enter the 4- and 6-positions of the 5-aminobenzo-2,1,3-thiodiazole (VIII) and (IX).



(VII) (VIII) (IX)

It has been shown previously [1-5] that on nitration and sulfonation the nitro and sulfo group, respectively, enter the 4-position of the aromatic ring, i.e., the thiodiazole ring directs the substituent in these reactions into the 4-position. On the basis of what has been stated it might be assumed that on chlorination or bromination of 5-aminobenzo-2,1,3-thiodiazole the chlorine or bromine would enter the position most favored by the joint orientation of the amino group and the thiodiazole ring, i.e., position 4. But actually, as we have shown, bromine (and probably chlorine) in this reaction replaces the hydrogen in the hydrocarbon ring in position 6.

Similarly in the bromination of benzo-2,1,3-thiodiazole-5-thiourea (X) the bromine also replaces the hydrogen on C_6; the bromine derivative formed (XI) is converted into the corresponding derivative of benzothiazole (XII).



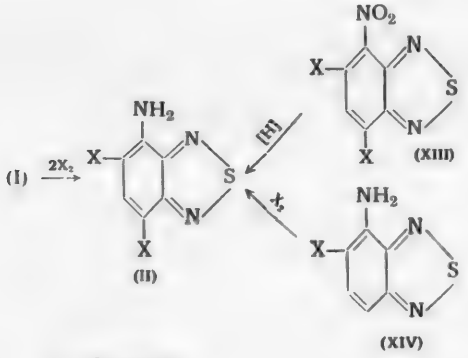
(X) (XI) (XII)

Since we have recently shown [4, 6] that benzo-2,1,3-thiodiazole, and also 1',2'-naphtho-2,3-thiodiazole [6] enter into an addition reaction with chlorine or bromine, it was of interest to investigate the halogenation (chlorination, bromination) of 4-aminobenzo-2,1,3-thiodiazole under conditions similar to those for the halogenation of the 2,1,3-thiodiazole derivatives mentioned.

For this purpose 4-aminobenzo-2,1,3-thiodiazole (I) was subjected to both chlorination and bromination in the fused state. The products isolated were 4-aminobenzo-5,7-dichloro- and 4-amino-5,7-dibromo-2,1,3-thiodiazole, respectively. Thus, when 4-aminobenzo-2,1,3-thiodiazole (fused) is reacted with chlorine or bromine a substitution reaction occurs, and not an addition, as is observed on reaction of benzo-2,1,3-thiodiazole (fused) with chlorine (or bromine).

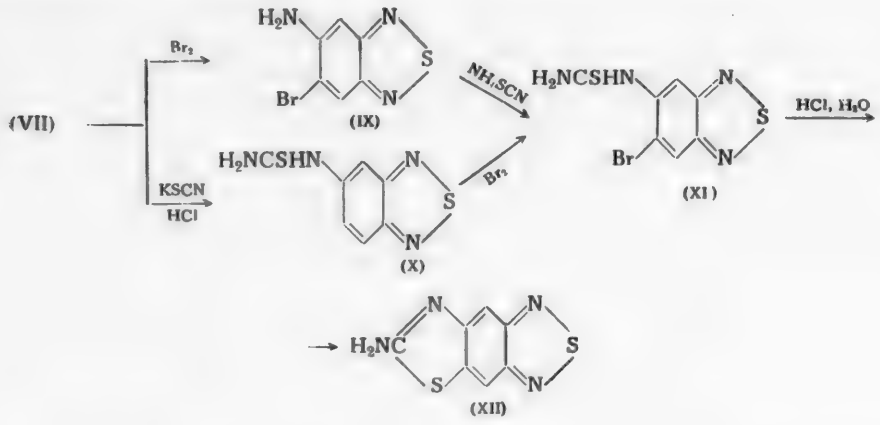
These and some other data show that the aromatic character of benzo-2,1,3-thiodiazole is intensified in its derivatives, for example in amino-, nitro-, and some halobenzo-2,1,3-thiodiazoles, while on the contrary the unsaturated character is weakened.

The structure of the halogenation products of 4-aminobenzo-2,1,3-thiodiazole, i.e., the position of the halogen, was proved by comparison of their properties with the properties of the reduction products of 5,7-dihalo-4-nitrobenzo-2,1,3-thiodiazole (XIII) and the halogenation products of 5-halo-4-aminobenzo-2,1,3-thiodiazole (XIV) [7].



X – halogen

The position of the bromine in (IX), the bromination product of (VII), was proved by conversion of the latter into 5,6-(2'-aminothiazole)benzo2,1,3-thiodiazole (XI) and identification of this derivative with the same compound obtained by the bromination of benzo-2,1,3-thiodiazole-5-thiourea (X).



Furthermore, this same compound (XI) was prepared by us from the thiocyanation product of 5-aminobenzo-2,1,3-thiodiazole, and also by the condensation of 2,5,6-triaminobenzothiazole with thionylaniline.

The chlorination of 4- and 5-aminobenzo-2,1,3-thiodiazoles was carried out with dichloramine in the presence of concentrated hydrochloric acid in acetic medium, and the bromination was conducted in acetic acid medium.

The derivatives of thiourea were synthesized by the reaction of the hydrochlorides of the appropriate amines with potassium thiocyanate or ammonium thiocyanate in chlorobenzene [8-12] or in water [13-17]. Cyclization of the thiourea derivatives was carried out by bromination of the latter in chloroform at 0° [13, 18]. As regards the starting 4- and 5-aminobenzo-2,1,3-thiodiazoles, they were synthesized in 85-87% yield by a reaction previously developed by us [19].

EXPERIMENTAL

4-Amino-5,7-dichlorobenzo-2,1,3-thiodiazole. a) Chlorination with dichloramine in acetic acid solution. To 1 g of 4-aminobenzo-2,1,3-thiodiazole, m. p. 68°, in 7 ml of 98% acetic acid and 1.65 g of dichloramine at 12° was added with continuous stirring over a period of 15 minutes a solution of 2 ml of concentrated hydrochloric acid in 7 ml of acetic acid. After 1 hour's stirring the precipitate that had separated was filtered off and washed in succession with a small amount of acetic acid and water. 1.15 g of a yellow crystalline material (80%) was obtained. After recrystallization from alcohol the crystals melted at 172.5-173° and gave no depression in a mixed melting point test with the reduction product of 4-nitro-5,7-dichlorobenzo-2,1,3-thiodiazole.

b) Chlorination in the fused state with gaseous chlorine. Chlorine was passed into a fusion of 4-aminobenzo-2,1,3-thiodiazole (0.5 g) to saturation; after the reaction mass was cooled, 0.7 g of a dark brown material was obtained, which after recrystallization from 50% alcohol (in the presence of carbon) melted at 171-173°. A mixed melting point test with known 4-amino-5,7-dichlorobenzo-2,1,3-thiodiazole showed no depression.

4-Amino-5,7-dibromobenzo-2,1,3-thiodiazole. a) Bromination in acetic acid solution. To 0.5 g of 4-aminobenzo-2,1,3-thiodiazole, m. p. 68°, in 10 ml of acetic acid was added from a dropping funnel with constant stirring a solution of 0.4 ml of bromine in 11 ml of acetic acid. After 1 hour's stirring the precipitate that had separated was filtered off, washed with acetic acid and water, and recrystallized from 50% alcohol; 1.07 g of yellow crystals, m. p. 163-164°, were obtained. A mixed melting point test with the reduction product of 4-nitro-5,7-dibromobenzo-2,1,3-thiodiazole showed no depression.

b) Bromination in the fused state. To 1 g of fused 4-aminobenzo-2,1,3-thiodiazole, m. p. 68°, was added at 70-75° 1.1 ml of bromine, the mixture was boiled for 2 hours, after which it was cooled and the excess bromine evaporated; 2.35 g of a dark mass was obtained, which after recrystallization from 50% alcohol (in the presence of carbon) melted at 164°. A mixed melting point test with the bromination product of 4-aminobenzo-2,1,3-thiodiazole in acetic acid showed no depression.

5-Amino-6-chlorobenzo-2,1,3-thiodiazole. To 1 g of 5-aminobenzo-2,1,3-thiodiazole, m. p. 116°, in 6 ml of acetic acid was added with stirring 0.83 g of dichloramine and then from a dropping funnel, gradually, a solution of 2 ml of concentrated hydrochloric acid in 4 ml of acetic acid. After 40 minute's stirring the precipitate that had separated was filtered off and washed consecutively with acetic acid and water. 0.89 g of material was obtained that melted after recrystallization from hot water at 152.5°. A mixed melting point test with the reduction product of 4-nitro-5-chlorobenzo-2,1,3-thiodiazole (m. p. 92°) showed a depression (92-102°).

Found %: N 22.74, 22.51; Cl 19.24, 19.32. $C_6H_4N_3SCl$. Calculated %: N 22.64; Cl 19.14.

5-Amino-6-bromobenzo-2,1,3-thiodiazole. To 1 g of 5-aminobenzo-2,1,3-thiodiazole, m. p. 116° in 6 ml of acetic acid was added a solution of 0.4 ml of bromine in 6 ml of acetic acid over a period of 30 minutes at 20°. After 1 hour's stirring the precipitate that had separated was filtered off and washed with acetic acid and water. 1.46 g of crystals were obtained that melted after recrystallization from hot water at 126-127°. A mixed melting point test with the reduction product of 4-nitro-5-bromobenzo-2,1,3-thiodiazole (m. p. 114°) showed a depression (the mixture melted at 85-95°).

Found %: N 17.36, 17.18; Br 35.00, 34.65; S 12.87, 13.18. $C_6H_4N_3SBr$. Calculated %: N 18.26; Br 34.78; S 13.91.

Benzo-2,1,3-thiodiazole-4-thiourea. A mixture of 2.9 g of the hydrochloride of 4-aminobenzo-2,1,3-thiodiazole (obtained by saturation of an ether solution of the base with hydrogen chloride), 1.5 g of ammonium thiocyanate, and 50 ml of chlorobenzene was heated with stirring for 10 hours on a boiling water bath, after which the reaction mass was cooled and the precipitate was filtered off and washed consecutively with chlorobenzene and water. 1.85 g of a material was obtained that melted after recrystallization from 50% alcohol at 200° (with decomp.); yield 60%.

Found %: C 40.21, 39.89; H 3.31, 2.86; N 26.55, 26.29. $C_7H_6N_4S_2$. Calculated %: C 40.00; H 2.86; N 26.67.

7-Bromo-4,5-(2'-aminothiazole)benzo-2,1,3-thiodiazole. In a 50 ml three-necked flask fitted with a stirrer, reflux condenser, and dropping funnel were placed 0.85 g of benzo-2,1,3-thiodiazole-4-thiourea, m. p. 183°, and 100 ml of chloroform. To the mixture was added at 0° with stirring over a period of 45 minutes 1.5 g of bromine in 9 ml of chloroform, after which the reaction mass was stirred (at 0°) for another 75 minutes and then left overnight (the reaction was accompanied by evolution of hydrogen bromide). The precipitate was filtered off and washed with chloroform. 1.5 g was obtained of a material with an extended melting point. The reaction product was heated to boiling with a mixture of 50 ml of hydrochloric acid (d 1.19), 400 ml of water, and carbon, the hot solution was filtered, and an excess of 25% ammonia solution was added to the clear, hot filtrate. The precipitate that separated was filtered off and washed with water. Yellow crystals were obtained, m. p. 302° (with decomp.).

Found %: N 19.22, 19.64; Br 28.24, 27.93. $C_7H_3N_4S_2Br$. Calculated %: N 19.51; Br 27.87.

5,6-(2'-Aminothiazole)benzo-2,1,3-thiodiazole. 1) Benzo-2,1,3-thiodiazole-5-thiourea. a) A mixture of 2.75 g of the hydrochloride of 5-aminobenzo-2,1,3-thiodiazole (obtained by saturation of an ether solution of the base with dry hydrogen chloride), 1.5 g of ammonium thiocyanate, and 20 ml of chlorobenzene was heated with stirring on a boiling water bath for 8 hours; after cooling, the precipitate was filtered off and washed consecutively with chlorobenzene and water. 1.55 g was obtained of a material, m. p. 193° (with decomp.); yield ~60%.

b) A solution of 1 g of 5-aminobenzo-2,1,3-thiodiazole, m. p. 116°, and 1 g of potassium thiocyanate in 10 ml of hydrochloric acid (d 1.04) was heated on a boiling water bath for 15 hours. The reaction product (a liquid with a yellow precipitate) was concentrated, the residue was heated for 2 hours to 102-108°, cooled, treated with water, and the precipitate was filtered off and washed with water. 1.35 g of a material was obtained, m. p. 193° (with decomp.); yield almost quantitative. After recrystallization from 50% alcohol gray crystals were obtained, m. p. 200° (with decomp.).

Found %: C 39.53, 40.30; H 2.78, 2.95; N 26.43, 26.82. $C_7H_6N_4S_2$. Calculated %: C 40.00; H 2.86; N 26.27.

2) 5,6-(2'-Aminothiazole)benzo-2,1,3-thiodiazole. a) To a mixture of 0.55 g of benzo-2,1,3-thiodiazole-5-thiourea, m. p. 200° (with decomp.), and 7 ml of chloroform was added over the course of 45 minutes at 0° with stirring a solution of 0.5 g of bromine in 5 ml of chloroform (the reaction was accompanied by the evolution of hydrogen bromide), and stirring at 0° was continued for 2 hours more. The precipitate (0.85 g) was filtered off, washed with chloroform, boiled for 1/2 hour with a mixture of 90 ml of water, 10 ml of hydrochloric acid (d 1.19) and carbon, and the hot solution was filtered. To the hot solution was added an excess of ammonia solution. The precipitate that separated was filtered off and washed with water. After the crystals were dried, they melted at 261-262° and showed no depression with known material.

b) A solution of 0.75 g of 5-amino-6-bromobenzo-2,1,3-thiodiazole, m. p. 126-127°, in 50 ml of chlorobenzene was saturated with dry hydrogen chloride, and the excess of this was expelled with dry air. To a suspension of the hydrochloride that was formed was added 0.3 g of ammonium thiocyanate, and the mixture was heated on a boiling water bath for 8 hours (until the hydrogen bromide was removed). On cooling, the precipitate was filtered off, washed with chlorobenzene and water, boiled with a mixture of 90 ml of water, 10 ml of concentrated hydrochloric acid, and carbon, and the hot solution was filtered and treated with a solution of ammonia. The precipitate that separated was filtered off and washed with water. The crystals melted at 259-261° and showed no depression in a mixed melting point test with the material previously prepared.

4- and 5-Aminobenzo-2,1,3-thiodiazoles. a) 4-Aminobenzo-2,1,3-thiodiazole. 90 g of iron filings and 400 ml of water were heated to boiling, and 8 ml of 98% acetic acid and 26 g of 4-nitrobenzo-2,1,3-thiodiazole m. p. 105°, were added. After the mixture had been boiled with energetic stirring for 20 minutes and cooled, the precipitate (reaction product and iron sludge) was filtered off, washed with a small amount of water, and extracted with ether; 18.9 g of 4-aminobenzo-2,1,3-thiodiazole was obtained (87%), which after recrystallization from hot water melted at 68° [19].

b) 5-Aminobenzo-2,1,3-thiodiazole. Reduction of 5-nitrobenzo-2,1,3-thiodiazole, m. p. 127-128°, was carried out under conditions similar to the preceding; yield 85-87%, m. p. 116°. The product formed yellow needles, soluble in organic solvents and in hot water; solubility in the latter was higher than that of 4-aminobenzo-2,1,3-thiodiazole.

Found %: S 21.64; N 27.34. $C_6H_5N_3S$. Calculated %: S 21.19; N 27.61.

SUMMARY

1. It has been shown that upon chlorination of 4-aminobenzo-2,1,3-thiodiazole with dichloramine, 4-amino-5,7-dichlorobenzo-2,1,3-thiodiazole is formed in good yield; upon bromination of 4-aminobenzo-2,1,3-thiodiazole with bromine in acetic acid 4-amino-5,7-dibromobenzo-2,1,3-thiodiazole also is formed in good yield (80% and more).

2. It has been shown that 4-amino-5,7-dichloro- and 4-amino-5,7-dibromobenzo-2,1,3-thiodiazoles, respectively, are also formed by the treatment of fused 4-aminobenzo-2,1,3-thiodiazole with chlorine or bromine.

3. It has been shown that 5-amino-6-bromobenzo-2,1,3-thiodiazole is produced by the bromination of 5-aminobenzo-2,1,3-thiodiazole; by chlorination (with dichloramine) of 5-aminobenzo-2,1,3-thiodiazole, 5-amino-6-chlorobenzo-2,1,3-thiodiazole (supposedly) is produced.

4. It has been shown that when 4- and 5-aminobenzo-2,1,3-thiodiazoles are reacted with thiocyanic acid, benzo-2,1,3-thiodiazole-4-thiourea and benzo-2,1,3-thiodiazole-5-thiourea are formed, respectively, and are cyclized on bromination to the corresponding benzothiazole derivatives.

5. A practicable method has been found for the synthesis of 5,6-(2'-aminothiazole)benzo-2,1,3-thiodiazole both by the reaction of 5-amino-6-bromobenzo-2,1,3-thiodiazole with thiocyanic acid and by the bromination of benzo-2,1,3-thiodiazole-5-thiourea.

LITERATURE CITED

[1] A. M. Khaletskii and V. G. Pesin, J. Gen. Chem. 24, 133 (1954).*

[2] M. L. Peyron, Bull. Soc. Chim. (5), 15, 502 (1948).

[3] A. M. Khaletskii, V. G. Pesin and Chao Chih-Chung, Proc. Acad. Sci. USSR, 106, 88 (1956).*

[4] V. G. Pesin, A. M. Khaletskii and Chao Chih-Chung, J. Gen. Chem. 27, 1570 (1957).*

[5] L. S. Efros and R. M. Levit, J. Gen. Chem. 25, 199 (1955).*

[6] Chao Chih-Chung, Dissertation, LKhFI (1956).**

[7] V. G. Pesin and A. M. Khaletskii, J. Gen. Chem. 27, 2599 (1957).*

[8] Synth. Org. Prep. Coll. 4, 512 (1953).

[9] Synth. Org. Prep. Coll. 3, 49 (1952).

[10] S. G. Ryklis and R. P. Vel'tman, Ukr. Chem. J. 18, 102 (1952).

[11] R. P. Vel'tman and S. G. Ryklis, Ukr. Chem. J. 20, 73 (1954).

[12] R. P. Vel'tman, Ukr. Chem. J. 21, 344 (1955).

[13] I. I. Levkoev, N. N. Sveshnikov, N. S. Barvyn' and M. P. Pashin, J. Gen. Chem. 22, 516 (1952).*

[14] R. Ebderfield and E. Schort, J. Org. Ch. 18, 1092 (1953).

[15] K. V. Vismanathan et al., J. Ind. Ist. Sci. 35, A, 251 (1953); Abstract Journal, Chemistry 139, 42970, No. 19 (1955).

[16] M. Ia. Shliakman and E. S. Vasserman, J. Appl. Chem. 27, 445 (1954).*

[17] Synth. Org. Prep. Coll. 4, 547 (1953).

*Original Russian pagination. See C. B. Translation.

**In Russian.

[18] Dorothy C. Schroeder, Chem. Revs. 55, 181 (1955).

[19] A. M. Khaletskii and V. G. Pesin, J. Gen. Chem. 20, 1914 (1950).*

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THE CHEMISTRY OF PROCESSES OF FAR-REACHING CHLORINATION OF PENTANE

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A number of investigators have studied the chlorination of pentane to mono- and disubstituted derivatives [1-6]. Very much less work has been devoted to the preparation of polychloropentanes containing more than two atoms of chlorine. Far-reaching chlorination of pentane has been effected photochemically [7] in a flow system in a medium of the reaction products (hexa- and heptachloropentanes). Reaction of tetrachloropentanes with chlorine has been studied at 370-500° under a pressure of some tens of atmospheres [8].

These conditions lead to considerable breakdown of the molecule. Chlorination of hexa-and heptachloropentanes has been studied at the ordinary pressure at 470° in an empty tube [7,9] as well as in a tube partly filled with infusorial earth impregnated with ferric chloride [10]. The temperature in the packed portion of the tube was 350-400° and that in the empty zone 450-500°. In both cases the main product of the reaction was hexachlorocyclopentadiene.

Formation of hexachlorocyclopentadiene on reaction of polychloropentanes with chlorine indicates that the carbon skeleton undergoes radical rearrangement with retention of the same number of carbon atoms. It has been suggested [7, 11] that chlorination, dehydrochlorination and cyclization take place in this case. The literature is lacking in experimental data concerning the mechanism of this process, which is also important for establishment of the theoretical bases of an industrial process of production of hexachlorocyclopentadiene. The latter is the principal intermediate for the production of a series of highly active insecticides, and it may find application in the industrial synthesis of other important compounds.

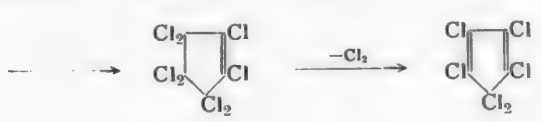
In the present work we studied the process of transformation of polychloropentanes into hexachlorocyclopentadiene.

Repetition of the literature methods of transformation of polychloropentanes into hexachlorocyclopentadiene led to formation of the desired product, of products of breakdown, and of an undistillable residue.

Study of these reaction products did not enable us to attack the problem of the mechanism of the processes involved since the use of a fairly high temperature allowed us to recover only the thermally stable compounds. We therefore made appreciable changes in the procedure for transformation of polychloropentanes. We chlorinated the latter in presence of infusorial earth at 350°. This caused a sharp fall in the yield of hexachlorocyclopentadiene but enabled the intermediate products to be isolated. Octachloropentadiene-1,3 and octachlorocyclopentene were found in the reaction mixture together with hexachlorocyclopentadiene and products of degradation. Formation of octachloropentadiene-1,3 evidently proceeds via nonachloropentenes and chlorination of polychloropentanes in alternating reactions of dehydrochlorination and addition of chlorine at the double bond.

The following scheme may be advanced for the conversion of polychloropentanes of normal structure into hexachlorocyclopentadiene:

$$C_5H_{12-n}Cl_n \xrightarrow{-(11-n)HCl} C_5HCl_9 \xrightarrow{-HCl} CCl_2{=}CCl{-}CCl{=}CCl{-}CCl_3 \rightarrow$$



Alternative schemes for conversion of polychloropentanes into hexachlorocyclopentadiene by a series of concurrent reactions can also be advanced. With the objective of checking the above scheme, we determined the material balance in the interaction of polychloropentanes with chlorine (see Table). In these experiments, which were run under various conditions, we obtained varying yields of reaction products, but we always observed a correspondence between the degrees of transformation of polychloropentanes as calculated from the carbon and hydrogen contents of the products.*

Degree of Transformation of Polychloropentanes ($C_5H_{5.5}Cl_{6.5}$) on Reaction with Chlorine, Calculated from the Carbon and Hydrogen Contents of the Reaction Products

Amt. polychloropentanes taken (g-moles)	HCl formed		Yield (%)						Deg. transformation polychloropentanes (%)	
	g-moles	g-moles/g-mole polychloropentane	CCl_4	C_2Cl_4	C_4Cl_6	C_5Cl_8	C_5Cl_8	cyclo-C_5Cl_8	from C	from H
1.112	5.34	4.79	0.9	1.4	2.5	20.6	6.5	55.5	87.4	87.0
0.556	2.61	4.70	0.9	0.5	7.0	21.6	10.7	46.9	87.6	85.5
1.112	5.27	4.74	0.9	2.6	2.1	29.2	2.8	50.4	88.0	86.0
1.112	5.42	4.86	1.1	3.8	5.6	31.6	5.0	40.6	86.7	88.5
1.112	5.20	4.66	1.3	4.2	1.9	60.4	3.5	11.7	83.0	85.0
0.556	2.09	3.75	0.4	1.6	11.7	32.2	15.0	8.2	69.1	68.4
0.400	1.92	4.80	3.6	0.7	1.5	45.0	16.7	16.8	84.3	87.0
1.112	5.10	4.69	0.4	1.3	8.3	53.7	12.2	12.6	88.5	83.5

Inspection of the table reveals a correspondence between the degrees of transformation of polychloropentanes calculated by the two independent methods. This correspondence indicates that we account for all of the main compounds formed in this process. The proposed scheme of transformations of polychloropentanes in presence of chlorine at high temperature is therefore the only one corresponding to the facts. Other possible schemes either do not apply or are realized to a negligible extent.

EXPERIMENTAL

Starting substances. Polychloropentanes were prepared by photochlorination of n-pentane. Constants of starting n-pentane: b. p. 36-37°, d_4^{20} 0.6252, n_D^{20} 1.3570.

Polychloropentanes form a transparent liquid with a lemon-yellow tinge; d_4^{20} 1.6584, n_D^{20} 1.5375; chlorine content 78%, corresponding to an average of 6.5 atoms of chlorine in the molecule.

Procedure. Chlorine was admitted from a cylinder via two flasks. The rate of flow of the chlorine was measured by a capillary flowmeter. Polychloropentanes were introduced from a dropping funnel. The reactor was a quartz tube, diameter 21 mm and length 1150 mm, filled with infusorial earth and placed in an electric furnace. Constant temperature was maintained in the furnace by means of a special system of regulating transformers. The temperature was measured with thermocouples. The reaction mixture entered a water condenser. Condensate formed was passed into a receiver, while the gases entered a trap maintained at −70°. An additional amount of liquid products of reaction collected in the trap. The gases passed from the trap into two columns (in series) for collection of hydrogen chloride and chlorine.

Analysis of the products of reaction. The hydrogen chloride content of the aqueous solutions was determined. The organic products of reaction were decanted and fractionally distilled in a flask fitted with a Vigreux column. At the start the chlorine and hydrogen chloride were eliminated by air-blowing at room temperature; after this, vacuum fractionation was carried out. We give the results of fractional distillation

* The degree of transformation of the carbon of polychloropentanes was determined as the sum of the yields of chlorocarbons formed. The degree of transformation of the hydrogen of polychloropentanes was determined as the ratio of the quantity of hydrogen chloride actually evolved in the process to the maximum quantity of hydrogen chloride that can be released on the assumption of exhaustive chlorination of the starting substances. Hydrogen was substantially absent from the organic products of transformation of polychloropentanes.

of the products of reaction in one experiment. 323 g of reaction mixture gave 9 g (2.8%) of chlorine and hydrogen chloride; the following liquid fractions were obtained:

1st, 3.5 g (1.1%), up to 82° (200 mm), d_4^{20} 1.6158, n_D^{20} 1.5038; 2nd, 16.4 g (5.1%) 82-110° (200 mm), d_4^{20} 1.6713, n_D^{20} 1.5370; 3rd, 8.5 g (2.6%), 110-112° (35 mm), d_4^{20} 1.6920, n_D^{20} 1.5568; 4th, 99.5 g (30.8%), 92-95° (4.5 mm), d_4^{20} 1.7044, n_D^{20} 1.5645; 5th, 36.7 g (11.4%), 95-100° (4.5 mm), d_4^{20} 1.7112, n_D^{20} 1.5655; 6th, 18.2 g (5.6%), 105-123° (4.5 mm), d_4^{20} 1.7447, n_D^{20} 1.5668; 7th, 11.9 g (3.7%), 123-125° (4.5 mm), d_4^{20} 1.7876, n_D^{20} 1.5720; 8th, 99.6 g (30.8%), 125-126° (4.5 mm), d_4^{45} 1.8064, n_D^{45} 1.5671; residue 11.6 g (3.6%).

The 7th fraction was subjected to further fractionation. The substance isolated had the constants: m. p. −77°, b. p. 100-102° (1.5 mm), d_4^{20} 1.7732, n_D^{20} 1.5708; these correspond to the literature data for octachloro-1,3-pentadiene [12]: m. p. −78°, b. p. 117° (3 mm), d_{15}^{25} 1.7664, n_D^{20} 1.5700.

Found %: C 17.8; Cl 82.1. C_5Cl_8. Calculated %: C 17.5; Cl 82.5.

Octachloro-1,3-pentadiene was passed together with chlorine through a reaction tube at 350° filled with infusorial earth. The main product of the reaction was octachlorocyclopentene (yield 75%); a small quantity of hexachlorocyclopentadiene (yield 9%) was also formed. It is known [14] that octachloro-1,3-pentadiene isomerizes (cyclizes) at a moderate temperature (up to 100°) to octachlorocyclopentene in presence of aluminum chloride.

The 8th fraction was recrystallized from alcohol. The compound isolated had the constants: m. p. 39°, b. p. 117° (3 mm), d_4^{45} 1.8189, n_D^{45} 1.5679, corresponding to the literature data for octachlorocyclopentene [12]: m. p. 38°, b. p. 107° (1.6 mm), 134° (6 mm), d_{15}^{45} 1.816, n_D^{45} 1.5683.

Found %: C 17.8; Cl 82.3. C_5Cl_8. Calculated %: C 17.5; Cl 82.5.

The isolated substance was passed through an empty tube at 500° to give hexachlorocyclopentadiene, an equimolar quantity of chlorine and unchanged starting substance. It is known [12, 13] that at 325-500° octachlorocyclopentene changes into hexachlorocyclopentadiene. The same process also takes place in the absence of catalyst at temperatures above 260° [15].

SUMMARY

1. Reaction of polychloropentanes of normal structure with chlorine was effected under conditions permitting isolation of the main intermediate products of transformation of the starting compounds into hexachlorocyclopentadiene. Under these conditions octachloro-1,3-pentadiene and octachlorocyclopentene were isolated and identified.

2. It was shown that the transformation of polychloropentanes into hexachlorocyclopentadiene proceeds according to the scheme: polychloropentanes → nonachloropentenes → octachloro-1,3-pentadiene → octachlorocyclopentene → hexachlorocyclopentadiene.

LITERATURE CITED

[1] A. F. Dobrianskii and Ia. Gurevich, Petrol. Economy 15, 352 (1928).

[2] A. F. Dobrianskii, M. Davydova and E. Margules, J. App. Chem. 6, 1123 (1933).

[3] E. Bertyporoch, Ber. 66, 732 (1933).

[4] T. D. Stewart and B. Weidenbaum, J. Am. Chem. Soc. 57, 1702 (1935).

[5] A. Lemke and D. Tishchenko, J. Gen. Chem. 7, 1995 (1937).*

[6] S. S. Nametkin and A. G. Serebrennikova, Bull. Acad. Sci. USSR, Div. Chem. Sci. 695 (1944).

[7] E. T. McBee and C. F. Baranauskas, Ind. Eng. Ch. 41, 806 (1949).

[8] E. T. McBee, H. B. Hass and E. Pierson, Ind. Eng. Ch. 33, 181 (1941).

*Original Russian pagination. See C. B. Translation.

[9] U. S. Pat. 2509160 (1950); Ch. A. 44, 7871 (1950).

[10] U. S. Pat. 2650942 (1953); Ch. A. 48, 10066 (1954).

[11] N. N. Mel'nikov and L. G. Vol'fson, Chem. Ind. 1953, 413.

[12] J. A. Krynitsky and R. W. Bost, J. Am. Chem. Soc. 69, 1918 (1947).

[13] Brit. Pat. 703202 (1945); Ch. A. 49, 6995 (1955).

[14] H. J. Prins, Rec. trav. chim. 51, 1065 (1932).

[15] J. A. Krynitsky and H. W. Carhart, J. Am. Chem. Soc. 71, 816 (1949).

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THE REACTION OF PHOSPHORUS PENTACHLORIDE WITH ESTERS OF OXAMIC ACID

AMIDES OF ALKOXYDICHLOROACETIC ACIDS

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As was shown earlier [1], the action of phosphorus pentachloride on ethyl oxamate (oxamethane) gives in succession the amide of ethoxydichloroacetic acid and trichlorophosphazoethoxydichloroacetyl according to the equations

$$C_2H_5OCOCONH_2 + PCl_5 \longrightarrow POCl_3 + C_2H_5OCCl_2CONH_2 \quad (1)$$

$$C_2H_5OCCl_2CONH_2 + PCl_5 \longrightarrow 2HCl + C_2H_5OCCl_2CON{=}PCl_3 \quad (2)$$

The preparation of trichlorophosphazoethoxydichloroacetyl and its analogs has been studied fairly closely and it has been shown that reaction (2) is a general one for the synthesis of trichlorophosphazoalkoxydichloroacetyls [2]. It was of interest to establish whether reaction (1) is a general one and whether it can be utilized as a general method of preparation of amides of alkoxydichloroacetic acids.

It was found that reaction (1) goes with adequate speed at temperatures very much lower than in the case of reaction (2) for the methyl, ethyl, butyl and isobutyl esters of oxamic acid. This enabled us to obtain good yields of the corresponding alkoxydichloroacetic acids, although in all cases reaction (2) proceeds side by side with reaction (1). Quantitative separation of the amides of alkoxydichloroacetic acids and trichlorophosphazoalkoxydichloroacetyls is impossible, but the quantity of trichlorophosphazo compound formed can be estimated with facility from the quantity of hydrogen chloride evolved whose determination is remarkably simple. It was found that reaction (1) in the case of butyl and isobutyl esters of oxamic acid goes with a yield of about 90% at a temperature of -10 to -5° in the course of 20-30 minutes. Very little hydrogen chloride is evolved. Reaction of ethyl oxamate with phosphorus pentachloride according to equation (1) takes place only at a very much higher temperature (8 to 10°) in the course of 50-60 minutes, and the yield is about 70%. The reaction is accompanied by evolution of about 10% of hydrogen chloride according to equation (2). Methyl oxamate reacts with phosphorus pentachloride with even greater difficulty. At 10° the reaction takes 3 hours and is accompanied by release of about 20% of hydrogen chloride according to equation (2). The yield of amide of methoxydichloroacetic acid is only 60-64%. Consequently, reaction (1) proceeds the most sluggishly in the case of methyl oxamate, more easily with ethyl oxamate, and very easily with the butyl and isobutyl esters.

Amides of dichloroaroxyacetic acids could not be obtained from aryl esters of oxamic acid [3] (phenyl, tolyl, p-chlorophenyl, p-nitrophenyl and naphthyl). Reaction of 1 mole of phosphorus pentachloride and 1 mole of aryl esters of oxamic acid gives a mixture of the corresponding trichlorophosphazoaroxydichloroacetyl and unreacted aryl ester of oxamic acid. The result is the same if less phosphorus pentachloride is used, but more of the ester of oxamic acid remains unchanged. Consequently, equation (2) goes more rapidly than (1) in the case of aryl esters of oxamic acid, and therefore this scheme cannot lead to amides of aroxydichloroacetic acids.

The practical impossibility of obtaining amides of aroxydichloroacetic acids may be due either to slowing down of reaction (1) or to acceleration of reaction (2), or to both of these causes. It is well-known that

the oxygen atom linked to carbon by a weakly polarized double bond (in aldehydes, ketones and esters of oxalic acid) is relatively easily replaced by two atoms of chlorine under the action of phosphorus pentachloride [4]. Under the same conditions the oxygen atom linked to the carbon atom by a very much more strongly polarized double bond (in esters of carboxylic and many other acids) is not replaced by two atoms of chlorine. Consequently, increased polarization of a double bond >C=O undoubtedly hinders the replacement of an oxygen atom by two chlorine atoms under the action of phosphorus pentachloride. The probable reason is that polarization of a carbon–oxygen double bond hinders the formation of an intermediate product of addition of the $[PCl_4]^+$ ion to the oxygen atom, since the $>C=\overset{+}{O}-PCl_4$ grouping (unpolarized >C=O bond) is more advantageous than the $>\overset{+}{C}-O-PCl_4$ grouping (polarized $>\overset{+}{C}-\overline{O}$ bond). Isomerization of one grouping into the other is hindered by the same forces that promote polarization.

On the other hand, experiment shows that the rate of formation and, in particular, the stability of trichlorophosphazo compounds increase with increasing strength of the acid corresponding to the original amide. For example, the amide of trichloroacetic acid is readily converted into the exceptionally stable trichlorophosphazo compound [5]; a very much less stable trichlorophosphazo compound is obtained with greater difficulty from the amide of p-nitrobenzoic acid, a still less stable product is obtained from benzamide [6], and no product at all is obtained from acetamide. Replacement of alkyl by aryl in esters of oxamic acid is bound to increase the polarization of the double bond of >C=O in the ROCO– group; on the other hand replacement of alkyl by aryl must slow down reaction (1) and accelerate reaction (2), thus eliminating the possibility of formation of amides of aroxydichloroacetic acids as intermediates of the reaction. The same causes must accelerate reaction (1) and slow down reaction (2) on passing from methyl oxamate to higher aliphatic esters (observations confirm this), since methyl is the most electronegative of all the unsubstituted alkyls. However, the increase in yields of amides of alkoxydichloroacetic acids on transition from lower esters of oxamic acid to higher is also the consequence of the considerably lower stability of methoxydichloroacetamide in comparison with the amides of higher alkoxydichloroacetamides. This behavior is not due to the same cause, i.e., lowering of the electronegativity on transition from methyl to higher amides, but it makes clear why methyl and ethyl chlorides are split off very easily, while chlorobenzene is hardly ever split off.

Amides of alkoxydichloroacetic acids are colorless, crystalline substances with melting points higher than those of the corresponding trichlorophosphazoalkoxydichloroacetyls [2]. They are hydrolyzed by moist air with relative facility but with considerably greater difficulty than trichlorophosphazoalkoxydichloroacetyls. The halogen atoms in amides of alkoxydichloroacetic acids are very labile and are easily replaced by various groups. Heating of amides of alkoxydichloroacetic acids leads to their breakdown with formation of alkyl halides, hydrogen chloride, and solid products whose nature has not yet been established. Decomposition of amides of methoxy- and ethoxydichloroacetic acids is quantitative at relatively low temperatures (60-100°):

$$C_2H_5OCCl_2CONH_2 \longrightarrow C_2H_5Cl + HCl + C_2O_2NH$$

The solid substance obtained in the reaction is probably the product of further transformations of the initially formed oxalic acid imide or oxalic acid half nitrile.

Amides of butoxydichloroacetic acids decompose with incomparably greater difficulty when heated, due undoubtedly to the considerably greater facility of cleavage of methyl and ethyl chlorides in comparison with higher alkyl chlorides.

For this reason the amides of methoxy- and ethoxydichloroacetic acids are extraordinarily difficult to obtain in the pure state. They begin to split off alkyl halide with appreciable speed even at 60°, and they partly decompose during recrystallization. The results of nitrogen determinations on amides of methoxy- and ethoxydichloroacetic acids are therefore a little on the high side (see Experimental), while chlorine determinations on ethoxydichloroacetamide give results that are much too low, since decomposition of the substance by water or alkali solution causes a portion of the chlorine to volatilize as ethyl chloride. Results of analyses of amides of butoxy- and isobutoxydichloroacetic acids are in adequate agreement with the theoretical values.

The structure of the amides of alkoxydichloroacetic acids is fully confirmed by their reaction with phenols [3] according to the equation $NH_2COCCl_2OR + ArOH \longrightarrow NH_2COCOOAr + HCl + RCl$

and by the transformation of methoxydichloroacetamide into diphenoxymethoxyacetamide (yield about 75%) according to the equation $CH_3OCCl_2CONH_2 + 2NaOC_6H_5 \rightarrow 2NaCl + CH_3OC(OC_6H_5)_2CONH_2$

EXPERIMENTAL

All of the starting substances and the solvents used for the syntheses described below must be thoroughly purified.

Methoxydichloroacetamide (I). Twenty-five ml of carbon tetrachloride and 0.1 mole of finely pulverized methyl oxamate were placed in a flask fitted with a stirrer and thermometer and attached to a reflux condenser which was connected in succession to a small bubble counter containing a few drops of sulfuric acid and a hydrogen chloride trap containing 250 ml of water. The mixture was cooled to 5°, 0.1 mole of finely pulverized phosphorus pentachloride was added quickly, the stirrer was started, and the temperature was held at 8-10°. (Since at lower temperatures the reaction goes extremely slowly, while at higher temperatures the quantity of liberated hydrogen chloride is sharply reduced [reaction (2) is accelerated]). The phosphorus pentachloride gradually goes into solution, hydrogen chloride is slowly evolved, and (I) soon starts to come out of solution in the form of colorless scales. The reaction is completed in 3 hours. This is indicated by the disappearance of the yellow grains of phosphorus pentachloride and by cessation of evolution of hydrogen chloride. 0.03-0.04 mole of hydrogen chloride in all was liberated or 15-20% of the quantity calculated from equation (2). (I) was suction-filtered, washed with ligroine (2 × 3 ml) and dried in vacuo at room temperature. Yield 9-10 g (60-64%); m. p. 95-96°. After recrystallization from benzene (9 g 50 ml, heating for only a short period), the melting point and elementary composition did not change.

Found %: N 9.78, 9.48. Equiv. after hydrolysis 2.70, 2.78. $C_3H_5O_2NCl_2$. Calculated %: N 8.90. Equiv. after hydrolysis 3.00.

The substance is slowly hydrolyzed by water at room temperature and rapidly on boiling; it is very easily soluble in dioxane and acetone, easily soluble in dichloroethane; it can be recrystallized, with partial decomposition, from benzene and carbon tetrachloride; it is sparingly soluble in boiling ether and ligroine.

Thermal cleavage of (I). (I) slowly splits off methyl chloride when kept in vacuo at room temperature. The reaction is much faster at 60°, while at 100° it is completed in 2 hours and 86% of the methyl chloride comes off (b. p. -24°).

Conversion of (I) into phenyl oxamate. See [3].

Conversion of (I) into diphenoxymethoxyacetamide (monomethyl-diphenyl orthoester of oxamic acid) (II). To a mixture of 0.04 mole of sodium phenate and 50 ml of benzene was added 0.02 mole of (I) with vigorous stirring. The reaction goes with liberation of heat. After 30 minutes the mixture was heated to the boil, and the separated sodium chloride was filtered off. On cooling, the solution deposited (II) in the form of colorless, fine crystals. M. p. 157-159° after recrystallization from benzene. Yield 70-73%. (II) is tasteless and odorless, insoluble in water and 0.1 N alkali, sparingly soluble in boiling carbon tetrachloride and ligroine; it can be recrystallized from alcohol, ether and benzene.

Found %: N 5.26, 5.08. $C_{15}H_{15}O_4N$. Calculated %: N 5.13.

Ethoxydichloroacetamide (III) was prepared in the same manner as (I). At 8-10° the reaction is completed in 50-60 minutes. About 10% of hydrogen chloride is released, calculated on equation (2). The reaction solution deposited 10-10.5 g of (III) with m. p. 80-82°. The mother liquor yielded a further 1-1.5 g of (III) after evaporation in vacuo at room temperature to a volume of 10 ml. Further evaporation leads to separation from the liquor of the secondary reaction product – trichlorophosphazoethoxydichloroacetyl. Total yield of (III) about 70%. M. p. 81-82° after recrystallization from carbon tetrachloride (10 g from 35 ml with only short-period heating); the composition was unchanged.

Found %: N 8.36, 8.40, 8.34, 8.53. Equiv. after hydrolysis 2.82, 2.84 (phenolphthalein); 1.90, 2.03 (methyl orange). $C_4H_7O_2NCl_2$. Calculated %: N 8.15. Equiv. after hydrolysis 3.00 (phenolphthalein), 2.00 (methyl orange).

Results of chlorine determinations (after hydrolysis with warm water) were 4-5% low.

(III) crystallizes in the form of fine, colorless prisms scarcely differing from (I) in solubility, but easily soluble in benzene and carbon tetrachloride. Heating to above 60° for several hours leads to quantitative breakdown of (III) into 1 mole of ethyl chloride, 1 mole of hydrogen chloride, and a solid substance of unknown structure. Treatment with phenols gives the corresponding esters of oxamic acid [3].

Butoxydichloroacetamide (IV). The reaction is completed in 20 minutes at a temperature of -5 to -10°; very little hydrogen chloride is released. (IV) goes completely into solution when the reaction mixture is brought to room temperature. After filtration through a dry filter, the solution was evaporated in vacuo (5 mm) at 30-40°. The residue contained (IV) in the form of a viscous oil which soon crystallized completely. Yield 90%; after recrystallization from ligroine (b. p. 90-95°), (IV) is obtained in the form of long, colorless needles; m. p. 57-59°. It is appreciably more soluble in common solvents than (III).

Found %: N 7.19, 7.36; Cl 35.00, 34.97. Equiv. after hydrolysis 3.11, 3.09. $C_6H_{11}O_2NCl_2$. Calculated %: N 7.00; Cl 35.48. Equiv. after hydrolysis 3.00.

Isobutoxydichloroacetamide (V) was obtained in the same manner as (IV). Yield 90%; it crystallizes from ligroine in the form of needles up to 10 mm in length; m. p. 76-78°. It hardly differs from (IV) in solubility.

Found %: Cl 35.41, 35.30. Equiv. after hydrolysis 3.07, 3.04. $C_6H_{11}O_2NCl_2$. Calculated %: Cl 35.48. Equiv. after hydrolysis 3.00.

Reaction of equimolar quantities of phosphorus pentachloride and aromatic esters of oxamic acid was studied with many substances under a great diversity of reaction conditions. In no case could the amides of the corresponding aroxydichloroacetic acids be obtained. These experiments are therefore not described in detail.

SUMMARY

Reaction of equimolar quantities of phosphorus pentachloride and aliphatic esters of oxamic acid gives amides of alkoxydichloroacetic acids. Amides of the corresponding aroxydichloroacetic acids could not be isolated from the products of reaction of phosphorus pentachloride with aromatic esters of oxamic acid.

LITERATURE CITED

[1] A. V. Kirsanov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1954, 646.*

[2] A. V. Kirsanov and V. P. Molosnova, J. Gen. Chem. 25, 772 (1955).*

[3] A. V. Kirsanov and V. P. Molosnova, J. Gen. Chem. 27, 3075 (1957).*

[4] R. Anschütz, Lieb. Ann. 254, 18 (1889).

[5] A. V. Kirsanov and G. I. Derkach, J. Gen. Chem. 26, 2009 (1956).*

[6] A. V. Kirsanov and R. G. Makitra, J. Gen. Chem. 26, 907 (1956).*

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DIESTERS OF ARYLAMIDOPHOSPHORIC ACIDS

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By analogy with diesters of arylsulfonamidophosphoric acids [1] diesters of arylamidophosphoric acids ought to be formed by the action of sodium arylates or alcoholates on the diacid chlorides of arylamidophosphoric acids according to scheme (1), or by saponification of triaroxyphosphazoacyls according to scheme (2).

$$ArCONHPOCl_2 + 2NaOR \longrightarrow 2NaCl + ArCONHPO(OR)_2 \quad (1)$$

$$ArCON{=}P(OR)_3 + H_2O \longrightarrow ROH + ArCONHPO(OR)_2 \quad (2)$$

The dimethyl ester of benzoylamidophosphoric acid is obtained according to scheme (1) in presence of excess of sodium methoxide and methyl alcohol in yield of 87%, but aromatic diesters are obtained by the same scheme (from dry phenolates) in yields not exceeding 10-25%. Changes in the reaction conditions, including the use of 3 moles of phenolate instead of 2, do not improve the yields. The reason for this is unknown, since the corresponding diesters of alkyl- and arylsulfonamidophosphoric acids are obtained by a similar scheme in very good yields [1].

Scheme (2) leads to very satisfactory yields of diaryl esters, and there is no need to isolate the easily saponified triaroxyphosphazoacyls [2]. We can start directly from trichlorophosphazoacyls [3] which react with dry sodium arylates in benzene, ether or dioxane solutions to give the corresponding triaroxyphosphazoacyls [2] according to the scheme

$$ArCON{=}PCl_3 + 3NaOR \longrightarrow 3NaCl + ArCON{=}P(OR)_3$$

Without separation of the precipitated sodium chloride, water is added to the resultant solution of triaroxyphosphazo compound, and the mixture is refluxed.

Triaroxyphosphazoacyls are hydrolyzed to diesters with incomparably greater facility than triaroxyphosphazosulfonaryls [1], and 5-10 minutes' heating with water is sufficient for complete transformation of triaroxyphosphazoacyls into diaryl esters of acylamidophosphoric acids.

p-Chlorobenzonitrile is sometimes isolated as a by-product in the preparation of diesters of p-chlorobenzoylamidophosphoric acid; it is formed by thermal cleavage of triaroxyphosphazo-p-chlorobenzoyls [2] or of diaryl esters of p-chlorobenzoylamidophosphoric acid; this cleavage process evidently goes parallel with reaction (2).

Scheme (2) gave the methyl, phenyl, p-cresyl, p-chlorophenyl and o- and p-nitrophenyl esters of benzoyl-, p-chlorobenzoyl- and p-nitrobenzoylamidophosphoric acids and the di-α-naphthyl ester of benzoylamidophosphoric acid.

All of the diesters, with the exception of the nitrophenyl esters, are colorless crystalline substances, melting in the range of 116-196°, insoluble in water, sparingly soluble in ether and ligroine, easily soluble in benzene, acetone, chloroform and dioxane. The aromatic diesters can be recrystallized from alcohol, carbon tetrachloride, and ligroine. The dimethyl esters are readily soluble in alcohol and can be recrystallized from water, carbon tetrachloride and mixtures of benzene and ligroine.

Dinitrophenyl esters of acylamidophosphoric acids are colorless or faint-yellow crystalline substances, melting over the range of 151-180°, insoluble in water and common organic solvents except dioxane. They can be recrystallized from a mixture of dioxane and alcohol.

All of the diesters of acylamidophosphoric acids are monobasic acids. The dimethyl esters titrate exactly in presence of phenolphthalein in aqueous solutions; all of the others, except the nitrophenyl esters, titrate in aqueous alcoholic or alcoholic solutions. Only the dimethyl esters dissolve easily in aqueous solutions of caustic alkalies; all of the others are very sparingly soluble due to the poor solubility of the salts. The nitro esters could not be titrated because the solutions of their salts are very strongly colored. Heating of the nitro esters with aqueous alcoholic caustic alkali brings them into solution, and the sodium salts of the diesters come down, after cooling, in the form of brightly colored needles. On treatment with dilute acids, these salts are transformed into the original dinitrophenyl esters.

EXPERIMENTAL

Dimethyl benzoylamidophosphate (I). To a cooled solution of 0.03 mole of sodium methoxide in 15 ml of methanol was added portionwise 0.01 mole of pulverized diacid chloride of benzoylamidophosphoric acid (II). Addition of each portion was marked by strong heat development or even by boiling up of mixture. After the whole of the (II) had been added, the mixture was refluxed for 15 minutes, after which the methanol was evaporated in vacuo. The residue was dissolved in water, and the solution was filtered and acidified with hydrochloric acid. (I) came down in the form of colorless platelets; yield 87%; m. p. 116-117°; the m. p. rose to 116-118° after recrystallization from a 1:1 mixture of benzene and ligroine or from 20% aqueous alcohol.

Found %: N 6.01. Equiv. 1.050. $C_9H_{12}O_4NP$. Calculated %: N 6.11. Equiv. 1.000.

Di-p-cresyl benzoylamidophosphate (III). To 0.04 mole of finely pulverized, thoroughly dried sodium cresylate was added 50 ml of dry dioxane and 0.02 mole of (II). Heat was developed on mixing. The reaction mixture was refluxed for 15 minutes, the dioxane was distilled off in vacuo, the residue was treated with water for removal of sodium chloride, and the precipitated oil was separated and dissolved in 80% alcohol with heating. On cooling, (III) came down in the form of colorless plates; yield 26%; m. p. 146-147°.

Found %: N 3.51. $C_{21}H_{20}O_4NP$. Calculated %: N 3.67.

(III) is obtained in 33.8% yield when (II) is heated with sodium cresylate in 1:3 molar ratio in benzene solution.

Di-p-chlorodiphenyl benxoylamidophosphate (IV) was obtained in the same manner as (III); colorless needles; yield 28.5%; m. p. 131-133°

Found %: N 3.26. $C_{19}H_{14}O_4NCl_2P$. Calculated %: N 3.31.

Di-p-nitrodiphenyl benzoylamidophosphate (V) was obtained in the same manner as (III); light-yellow prisms; m. p. 151-152°.

Found %: N 9.41. $C_{19}H_{14}O_8N_3P$. Calculated %: N 9.48.

Diphenyl benzoylamidophosphate (VI). To thoroughly dried and finely pulverized sodium phenolate (0.01 mole) was added in one portion a solution of 0.033 mole of trichlorophosphazobenzoyl in 80 ml of benzene. After the violent reaction had subsided, the mixture was refluxed with vigorous stirring for 15 minutes, after which 25 ml of water was added and the stirred mixture was boiled for another 5 minutes. On cooling, the benzene layer was separated, washed once with water, and filtered; the benzene was distilled off in vacuo. The residue contained an oily liquid which was dissolved in 5 ml of ether. (VI) quickly came down and was suction-filtered and washed with ether. It formed colorless needles after recrystallization from a 1:1 mixture of ligroine and ether; yield 65.1%; m. p. 147-149°.

Found %: N 3.96. Equiv. 1.002, 1.013. $C_{19}H_{16}O_4NP$. Calculated %: N 3.97. Equiv. 1.000.

Esters (III), (VII), (IV), (VIII)-(XIII), described below, were prepared in the same manner as (VI).

Di-p-cresyl benzoylamidophosphate (III); yield 52.4%; colorless plates after recrystallization from alcohol; m. p. 146-147°; no melting point depression in admixture with (III) obtained from (II).

Di-α-naphthyl benzoylamidophosphate (VII); yield 55.6%; sparingly soluble in cold benzene and therefore starts to come down even on washing of the benzene solution with water. Recrystallization from benzene gives tablets with m. p. 195-196°.

Found %: N 3.39. $C_{27}H_{20}O_4NP$. Calculated %: N 3.09.

Di-p-chlorophenyl benzoylamidophosphate (IV); yield 75.6%; it forms plates with m. p. 131-133° from a mixture of benzene and ligroine; no melting point depression in admixture with (IV) prepared from (II).

Diphenyl p-chlorobenzoylamidophosphate (VIII). When the synthesis is performed in benzene solution, p-chlorobenzonitrile is obtained as residue after the benzene has been distilled off; m. p. 94-95° [4]. Evidently, triphenoxyphosphazo-p-chlorobenzene or (VIII) is completely decomposed in boiling benzene solution. The yield is 34.4% when the synthesis is performed in a medium of ether, but an appreciable quantity of p-chlorobenzonitrile is then also obtained at the same time. Colorless prisms with m. p. 142-143° after recrystallization from alcohol.

Found %: N 3.85. $C_{19}H_{15}O_4NClP$. Calculated %: N 3.61.

Di-p-cresyl ester of p-chlorobenzoylamidophosphoric acid (IX); yield 31.3% (in benzene solution); colorless needles from alcohol; m. p. 139-140°.

Found %: N 3.53. $C_{21}H_{19}O_4NClP$. Calculated %: N 3.57.

Di-p-chlorodiphenyl p-chlorobenzoylamidophosphate (X); yield 74%; needles with m. p. 155-156° from alcohol.

Found %: N 3.18. $C_{19}H_{13}O_4NCl_3P$. Calculated %: N 3.07.

Diphenyl p-nitrobenzoylamidophosphate (XI); yield 89.1%; crystallizes from carbon tetrachloride or alcohol in the form of slender, light-yellow needles; m. p. 151-152°.

Found %: N 6.97. Equiv. 1.004, 0.958. $C_{19}H_{15}O_6N_2P$. Calculated %: N 7.04. Equiv. 1.000.

Di-p-cresyl p-nitrobenzoylamidophosphate (XII); yield 54.6%; light-yellow prisms from alcohol with m. p. 165-167°.

Found %: N 6.53. $C_{21}H_{19}O_6N_2P$. Calculated %: N 6.58.

Di-p-chlorodiphenyl p-nitrobenzoylamidophosphate (XIII); yield 79.5%; yellow prisms from alcohol; m. p. 175-176°.

Found %: N 6.03. $C_{19}H_{13}O_6N_2Cl_2P$. Calculated %: N 6.00.

Di-o-nitrodiphenyl benzoylamidophosphate (XIV). 0.02 mole of (II) was added quickly to a mixture of thoroughly dried sodium o-nitrophenate and 50 ml of dry benzene. Slight heat was generated on mixing. The stirred reaction mixture was boiled until nearly the whole of the nitrophenate had disappeared (about 1 hour). 25 ml of water was then added, and boiling and stirring were continued for another few minutes. After 24 hours, the precipitated (XIV) was suction-filtered, washed with water, alcohol and ether for removal of nitrophenol, and dried. Yield 90.7%. The product was purified by dissolution in a small volume of hot dioxane, filtration of the solution, and addition to it of twice the volume of alcohol. Light-yellow prisms came down on cooling; m. p. 154-155°.

Found %: N 9.53. $C_{19}H_{14}O_8N_3P$. Calculated %: N 9.48.

The esters (V), (XV)-(XVIII) were prepared in the same way as (XIV).

Di-p-nitrodiphenyl benzoylamidophosphate (V); yield 66%; light-yellow prisms from a mixture of dioxane and alcohol; m. p. 151-152°; no depression in admixture with (V) obtained from (II).

Di-o-nitrodiphenyl p-chlorobenzoylamidophosphate (XV); yield 62%; light-yellow needles; m. p. 179-180°.

Found %: N 8.70. $C_{19}H_{13}O_8N_3ClP$. Calculated %: N 8.80.

Di-p-nitrodiphenyl p-chlorobenzoylamidophosphate (XVI); yield 57.8%; light-yellow prisms; m. p. 167-168°.

Found %: N 8.93. $C_{19}H_{13}O_8N_3ClP$. Calculated %: N 8.80.

Di-o-nitrodiphenyl-p-nitrobenzoylamidophosphate (XVII); yields 84.6%, light-yellow prisms, m. p. 178-179°.

Found %: N 11.61. $C_{19}H_{13}O_{10}N_4P$. Calculated %: N 11.47.

Di-p-nitrodiphenyl p-nitrobenzoylamidophosphate (XVIII); yield 81.7%; light-yellow needles; m. p. 179-180°.

Found %: N 11.25. $C_{19}H_{13}O_{10}N_4P$. Calculated %: N 11.47.

Dimethyl benzoylamidophosphate (I). 0.025 mole of trichlorophosphazobenzoyl was added in small portions to a solution of 0.1 mole of sodium methoxide in 30 ml of methanol while cooling. The reaction was violent. After the whole of the trichlorophosphazobenzoyl had been added, the methyl alcohol was taken off in vacuo, the residue was dissolved in water, and the solution was filtered and acidified with hydrochloric acid. (I) came down as colorless plates; yield 56.5%; m. p. 116-118°. No change in melting point after recrystallization from 20% alcohol. No depression of melting point in admixture with (I) prepared from (II).

Esters (XIX) and (XX) were obtained from the corresponding trichlorophosphazoacyls in the same manner as (I).

Dimethyl p-chlorobenzoylamidophosphate (XIX); yield 90.9%; needles from 10% alcohol with m. p. 125-126°.

Found %: N 5.80. Equiv. 1.023. $C_9H_{11}O_4NClP$. Calculated %: N 5.92. Equiv. 1.000.

Dimethyl p-nitrobenzoylamidophosphate (XX); yield 87.3%; light-yellow needles from 50% alcohol with m. p. 153-154°.

Found %: N 10.19. $C_9H_{11}O_6N_2P$. Calculated %: N 10.22.

SUMMARY

A study was made of the reaction of diacid chlorides of arylamidophosphoric acids and of trichlorophosphazoacyls with sodium methoxide and sodium arylates. A series of diesters of arylamidophosphoric acids were prepared and their properties described.

LITERATURE CITED

[1] A. V. Kirsanov and V. I. Shevchenko, J. Gen. Chem. 24, 474, 882, 1980 (1954); 26, 504 (1956).*

[2] A. V. Kirsanov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1954, 646.*

[3] A. V. Kirsanov and R. G. Makitra, J. Gen. Chem. 26, 907 (1956).*

*Original Russian pagination. See C. B. Translation.

[4] Dictionary of Organic Compounds [Russian translation] (Foreign Lit. Press, 1949), Vol. I, p. 440.

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PREPARATION OF 2,4-DINITROPHENYL DERIVATIVES OF HYDROXY AND MERCAPTO COMPOUNDS AND AMINES

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The recommended procedure for the preparation of 2,4-dinitrophenyl derivatives for identification of hydroxy and mercapto compounds [1] is treatment of the latter with 2,4-dinitrochlorobenzene or 2,4-dinitrofluorobenzene in presence of various alkaline agents such as caustic alkalies [2, 3], sodium bicarbonate [4, 5], triethylamine [6] and a few other agents [7]. 2,4-Dinitrophenyl derivatives of amines are obtained by the interaction of equivalent quantities of amine and 2,4-dinitrochlorobenzene [1].

We showed earlier that 2,4-dinitrochlorobenzene reacts with hydroxy compounds in presence of anhydrous potassium fluoride with formation of ethers of 2,4-dinitrophenol [8]. It was found that the corresponding fluoro derivative (2,4-dinitrofluorobenzene) reacts with hydroxy compounds more smoothly in presence of anhydrous potassium fluoride than in presence of other bases. In this case the reaction goes from start to finish in a substantially neutral medium. In the case of primary alcohols and phenols, the pure 2,4-dinitrophenyl derivatives are obtained directly from the reaction mass in yields approaching the theoretical. The reaction goes according to the equation:

$$R{-}OH + F{-}C_6H_3(NO_2)_2 + KF \longrightarrow R{-}O{-}C_6H_3(NO_2)_2 + KHF_2$$

2,4-Dinitrophenyl derivatives of secondary hydroxy compounds are obtained in better yields in presence of of anhydrous potassium fluoride than in presence of the usually employed triethylamine. For example, the 2,4-dinitrophenyl derivative of N-phenyl-3-hydroxy-1,2,3,4-tetrahydroquinoline is obtained in 79% yield in presence of potassium fluoride, while in a parallel experiment using triethylamine the yield is only 28%. The 2,4-dinitrophenyl derivative of phenylmethyl carbinol is obtained in 28% yield with potassium fluoride (in a secondary reaction 12% of 2,2',4,4'-tetranitrodiphenyl ether is formed), whereas in presence of triethylamine the yield is only 11%. In this case the main product of the reaction is 2,2',4,4'-tetranitrodiphenyl ether (43%) whose formation is evidently due to the water liberated [8] by dehydration of phenylmethyl carbinol.

The literature [4] mentions that 2,4-dinitrophenol does not react with 2,4-dinitrofluorobenzene, 2,4-dinitrophenol and 2,4-dinitrofluorobenzene react in presence of potassium fluoride to give a substantially quantitative yield of 2,2',4,4'-tetranitrodiphenyl ether. p-Hydroxybenzoic acid gives a good yield of 2,4-dinitrophenyl derivative. The 2,4-dinitrophenyl derivative of salicylic acid could not be obtained. This contrasts with the behavior of its methyl ester.

Mercapto compounds are quantitatively converted into the 2,4-dinitrophenyl derivatives when heated with 2,4-dinitrochlorobenzene in presence of potassium fluoride. Products of adequate purity are obtained directly from the reaction mass.

$$R{-}SH + Cl{-}C_6H_3(NO_2)_2 + 2KF \longrightarrow R{-}S{-}C_6H_3(NO_2)_2 + KCl + KHF_2$$

Primary mercaptans react with 2,4-dinitrofluorobenzene even at room temperature in presence of potassium fluoride. 2,4-Dinitrophenyl derivatives of secondary mercaptans are obtained in somewhat lower yields. These derivatives are not easily obtained in the crystalline form, in agreement with the literature [3]. In

the absence of potassium fluroide, 2,4-dinitrochlorobenzene and 2,4-dinitrofluorobenzene do not react with mercapto compounds.

2,4-Dinitrophenyl derivatives of amines, prepared by reaction with 2,4-dinitrochloro- and 2,4-dinitrofluorobenzene in presence of potassium fluoride, are directly isolated from the reaction mass in the analytically pure form and in substantially quantitative yield.

Such a weakly basic amine as 2,4-dinitroaniline reacts with 2,4-dinitrochloro- and 2,4-dinitrofluorobenzene in presence of potassium fluoride at 120-130° to give 2,2',4,4'-tetranitrodiphenylamine in substantially quantitative yield (it was previously obtained in poor yield by heating 2,4-dinitrobromobenzene at 160° with 2,4-dinitroaniline in nitrobenzene in presence of potassium carbonate, potassium iodide and copper) [12].

The 2,4-dinitrophenyl derivative is quantitatively formed from anthranilic acid by the action of 2,4-dinitro derivative of both chlorobenzene and fluorobenzene in presence of potassium fluoride.

EXPERIMENTAL

Preparation of 2,4-dinitrophenyl derivatives of hydroxy compounds. 0.0025 mole of hydroxy compound was heated and stirred with the equivalent (0.47 g) of 2,4-dinitrofluorobenzene and 0.29 g (0.005 mole) of potassium fluoride [8] at 100-110°. The reaction mass was treated with hot benzene and filtered. The benzene was distilled off on a water bath, and the residue dissolved in a small quantity of boiling alcohol from which the 2,4-dinitrophenyl ether came down on cooling. Products so obtained are of adequate purity and their melting points as a rule are not raised after recrystallization (Table 1).

Reaction of N-phenyl-3-hydroxy-1,2,3,4-tetrahydroquinoline with 2,4-dinitrofluorobenzene in presence of triethylamine. 0.57 g of the hydroxy compound was heated (with stirring) for 5 hours with 0.47 g of 2,4-dinitrofluorobenzene and 3 drops of triethylamine at 100-110°. Crystallization of the reaction mixture from alcohol gave 0.27 g (28%) of derivative with m. p. 124°. A mixture with the product obtained in presence of potassium fluroide (m. p. 126°) melts at 124.5°.

Reaction of phenylmethyl carbinol with 2,4-dinitrofluorobenzene. 1) 1.22 g of phenylmethyl carbinol, 1.86 g of 2,4-dinitrofluorobenzene and 1.16 g of potassium fluoride were stirred for 2 hours at 140-150°. The reaction mass was treated with hot benzene and filtered. The benzene was driven off and the residue recrystallized from alcohol to give 0.21 g (12%) 2,2'4,4'-tetranitrodiphenyl ether (poorly soluble in hot alcohol) with m. p. 193° and 0.81 g (28%) of 2,4-dinitrophenyl derivative of phenylmethyl carbinol with m. p. 99°; the latter crystallizes as light-yellow needles.

Found %: N 9.82, 9.93. $C_{14}H_{12}N_2O_5$. Calculated %: N 9.71.

2) 0.43 g of phenylmethyl carbinol and 0.64 g of 2,4-dinitrofluorobenzene were stirred with 4 drops of triethylamine for 2 hours at 140-150°. The reaction mass was recrystallized from alcohol to give 0.26 g (43%) of 2,2',4,4'-tetranitrodiphenyl ether with m. p. 193° and 0.11 g (11%) of the 2,4-dinitrophenyl derivative of phenylmethyl carbinol with m. p. 97°. A mixture with the product obtained in the preceding experiment had m. p. 98°.

Reaction of 2,4-dinitrophenol with 2,4-dinitrofluorobenzene. 0.46 g of 2,4-dinitrophenol, 0.47 g of 2,4-dinitrofluorobenzene and 0.58 g of anhydrous potassium fluoride were stirred at 190-200° with 2 g of 2,4-dinitrochlorobenzene for 3 hours. The reaction mass was treated with hot water and filtered. The precipitate was repeatedly washed on the filter with water, then 3 times with alcohol (2 ml each time). In this manner 0.86 g (98%) of faintly yellowish, finely crystalline powder was obtained with m. p. 194.5°. The literature reports m. p. 195° [9]. A mixture with an authentic specimen of 2,2',4,4'-tetranitrodiphenyl ether did not give a depression of melting point.

Reaction of p-hydroxybenzoic acid with 2,4-dinitrofluorobenzene. 0.7 g of p-hydroxybenzoic acid, 0.93 g of 2,4-dinitrofluorobenzene and 0.58 g of potassium fluoride were stirred for 3 hours at 120-130°. The reaction mass turned yellow and towards the end of the experiment it solidified. The product was pulverized and washed with water, with hydrochloric acid (1 : 1) and twice with alcohol (2 ml each time). The product was purified by reprecipitation with water from 3 ml of concentrated sulfuric acid to give 1.4 g (93%) of substance with m. p. 254°. The melting point remained unchanged after recrystallization from acetic acid.

Found %: N 8.90, 9.03. $C_{13}H_8O_7N_2$. Calculated %: N 9.20.

Preparation of 2,4-dinitrophenyl derivatives of mercapto compounds. 0.0025 mole of mercapto compound was heated for 10-15 minutes at 100° with 0.51 g (0.0025 mole) of 2,4-dinitrochlorobenzene and 0.29 g (0.005 mole) of potassium fluoride. Ten ml of hot benzene was added to the reaction mass, and the mixture was filtered. The benzene was driven off on a water bath, and the residue was dissolved in a small quantity of boiling alcohol from which, on cooling, pure 2,4-dinitrophenyl derivative was deposited as yellow crystals (Table 2).

Reaction of n-butylmercaptan with 2,4-dinitrofluorobenzene. 0.23 g of n-butylmercaptan was stirred with 0.47 g of 2,4-dinitrofluorobenzene and 0.29 g of potassium fluoride. After a few minutes, the reaction mass turned yellow and solidified. Further treatment was similar to that described above. Yield 0.55 g (86%) of derivative with m. p. 66°.

TABLE 1

Reaction of Hydroxy Compounds with 2,4-Dinitrofluorobenzene

Hydroxy compound	Reaction period (hours)	% yield	Melting point	
			found	literature data
Ethyl alcohol*	1	93	85°	85° [6]
n-Octadecyl alcohol	5	81	65.5	65.5 [8]
1-Naphthol	0.5	97	127	128 [2]
2-Naphthol	0.5	93	94	95 [2]
p-Isooctylphenol	0.5	95	94.5 **	—
o-Hydroxydiphenyl	0.5	99	113 ***	—
p-Hydroxydiphenyl	0.5	95	116	118 [2]
Methyl salicylate	1	95	89	88 [7]
N-Phenyl-3-hydroxy-1,2,3,4-tetrahydroquinoline	5	79	126 ****	—

*Reaction was performed in excess of boiling alcohol (10 moles).

**White needles. Found %: N 7.52, 7.64. $C_{20}H_{24}O_5N_2$. Calculated %: N 7.53.

***White needles. Found %: N 8.29, 8.23. $C_{18}H_{12}O_5N_2$. Calculated %: N 8.32.

****Orange plates. Found %: N 10.75, 10.85. $C_{21}H_{17}O_5N_3$. Calculated %: N 10.73.

Reaction of sec-butylmercaptan with 2,4-dinitrofluorobenzene. 0.32 g of sec-butylmercaptan was stirred with 0.65 g of 2,4-dinitrofluorobenzene and 0.4 g of potassium fluoride for an hour at 90-100°. Further treatment was similar to that described above. Yield 0.61 g (69%) of product with m. p. 67.5°. The compound was isolated in the form of an oil which crystallized only after several days.

Found %: N 11.00, 10.85. $C_{10}H_{12}O_4N_2S$. Calculated %: N 10.92.

Preparation of 2,4-dinitrophenyl derivatives of amines. 1) 0.93 g of amine, 2.03 g of 2,4-dinitrochlorobenzene and 1.16 g of potassium fluoride were heated for 30 minutes at 100°; the solidified reaction mass was then pulverized, washed with water, with 5% hydrochloric acid again with water until the filtrate was free from chlorine ion, and finally with 2 ml of methyl alcohol. Yield 2.5 g (97%) with m. p. 156°. The literature [1] reports m. p. 156°. In a parallel experiment run without potassium fluoride, the product had m. p. 128-130°. The pure product could only be obtained by recrystallization from alcohol.

The same procedure for reaction of p-toluidine with 2,4-dinitrochlorobenzene in presence of potassium fluoride gave a product with m. p. 135°. The literature [1] reports m. p. 136°. In the absence of potassium fluoride the product had m. p. 116-120°.

2) 0.36 g of α-naphthylamine, 0.47 g of 2,4-dinitrofluorobenzene and 0.29 g of anhydrous potassium fluoride were heated for 10-15 minutes at 100°. Further treatment was on the same lines as described above. Yield 0.77 g (99%) of product with m. p. 191°. Literature: m. p. 191° [1].

The 2,4-dinitrophenyl derivative of β-naphthylamine was obtained in similar fashion. Yield 0.75 g (97%); m. p. 173° (the literature reports m. p. 179° [10] and m. p. 171° [11]). The melting point was unchanged after recrystallization from 1:1 mixture of benzene and alcohol.

Reaction of 2,4-dinitroaniline with 2,4-dinitrochlorobenzene and 2,4-dinitrofluorobenzene. 1) 0.46 g of 2,4-dinitroaniline was stirred with 0.51 g of 2,4-dinitrochlorobenzene and 0.29 g of potassium fluoride for 2.5 hours at 120-130°. The reaction mass turned red and solidified. The product was pulverized and washed with hot water. The color changed from red to yellow. Yield 0.85 g (97%). Recrystallization from aqueous acetone gave lustrous yellow plates with m. p. 199.5°. Literature: m. p. 199° [12].

2) Replacement of 2,4-dinitrochlorobenzene by 0.47 g of 2,4-dinitrofluorobenzene gave under the same conditions 0.86 g (99%) of product with m. p. 200° after recrystallization from aqueous acetone.

Reaction of anthranilic acid with 2,4-dinitrochlorobenzene. 0.34 g of anthranilic acid was stirred for 30 minutes with 0.51 g of 2,4-dinitrochlorobenzene and 0.29 g of potassium fluoride at 120-130°. The reaction mass turned red and solidified. The product was pulverized, washed with water and treated with 10% hydrochloric acid, after which it was washed many times with water and finally twice with methanol (2 ml each time). Yield 0.69 g (91%) with m. p. 259°. It formed yellow-needles, m. p. 262.5°, after recrystallization from a mixture of methyl alcohol and acetone. Literature: m. p. 262° [13].

0.34 g of anthranilic acid, 0.47 g of 2,4-dinitrofluorobenzene and 0.29 g of potassium fluoride similarly gave 0.74 g (97.5%) of product with m. p. 262°.

TABLE 2

Reaction of Mercapto Compounds with 2,4-Dinitrochlorobenzene

Mercapto compound	Yield of derivatives (%)	Melting point of derivatives	
		found	literature data [3]
p-Thiocresol	98	102.5°	103°
Thiophenol	97	120	121
p-Chlorothiophenol	97	123	123
n-Butylmercaptan	97	63	66

SUMMARY

A procedure for the preparation of 2,4-dinitrophenyl derivatives of hydroxy and mercapto derivatives and amines was developed; it consisted of treatment with 2,4-dinitrochlorobenzene and 2,4-dinitrofluorobenzene in presence of potassium fluoride.

LITERATURE CITED

[1] Johnson, Shannon and Reid, Organic Reagents for Organic Analysis [Russian translation] (For. Lit. Press, Moscow, 1948), pp. 58, 59, 136, 161, 162.

[2] R. Borst and F. Nicholson, J. Am. Chem. Soc. 57, 2368 (1935).

[3] R. Bost, J. Turner and R. Norton, J. Am. Chem. Soc. 54, 1985 (1932); R. Bost, J. Turner and M. Conn, J. Am. Chem. Soc. 55, 4956 (1933).

[4] H. Zahn and A. Würz, Z. anal. Ch. 134, 183 (1951).

[5] H. Kitano, K. Fukui and T. Osaka, J. Chem. Soc. Japan, Ind. Chem. Sect. 58, 119 (1955).

[6] W. Whalley, J. Chem. Soc. 1950, 2241.

[7] B. Tozer and S. Smiles, J. Chem. Soc. 1938, 2052.

[8] N. N. Vorozhtsov, Jr. and G. G. Iakobson, J. Gen. Chem. 27, 1672 (1957).*

[9] C. Willgerodt, Ber. 13, 887 (1880).

[10] O. Ernst, Ber. 23, 3429 (1890).

[11] H. Ryan and J. Drumm, Ch. A., 13, 563 (1919).

[12] H. Ryan and T. Glover, Ch. A. 12, 2543 (1918).

[13] F. Jourdan, Ber. 18, 1444 (1885).

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RADIOCHEMICAL INVESTIGATION OF REACTIONS OF ORGANOMETALLIC COMPOUNDS IN BENZENE SOLUTION

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With the help of deuterated benzene, G. A. Razuvaev, G. G. Petukhov, A. F. Rekasheva and G. P. Mikluk-hin [1] showed that diphenylmercury and phenylmercuric hydroxide behave differently in benzene solutions when irradiated with ultraviolet light. Whereas diphenylmercury reacts in the solvent a definitely radical mechanism with regeneration of the phenyl radicals, phenylmercuric hydroxide initially forms a reaction coil with the solvent.

In the present work a radiochemical method was used in a study of the behavior of diphenylmercury and phenylmercuric hydroxide in benzene solutions on photolysis and heating. Employment of a radiochemical procedure excluded the possibility of errors associated with hydrogen exchange between organometallic compounds and deuterated benzene. A radiochemical label in the form of radiocarbon was introduced into the benzene used as the reaction medium. Radioactive benzene was synthesized by the method of N. D. Zelinskii [2] from labeled acetylene prepared in turn from labeled barium carbide [3].

The activity of the original benzene and of the reaction products was determined with the help of an internally filled counter (carbon dioxide) [4]. The organic compound was previously burned to CO_2 in an oxygen stream using a micro method. Activities were measured with an accuracy of up to 3%.

A weighed sample of about 0.5 g of organometallic compound and 3-4 ml of labeled benzene with a specific activity of the order of 1.4×10^5 pulses/min. were placed in a quartz test tube which was then sealed and exposed to the light from a quartz mercury lamp. The period of irradiation varied between 50 and 150 hours. Thermal decomposition was effected in the same test tubes at 170-190° for 70-130 hours.

The reaction products were fractionated by the procedure previously recommended in a study of the photolysis of diphenylmercury and diphenylmercuric hydroxide in deuterated benzene. In a number of experiments the photolysis and thermal breakdown were not continued to the stage of complete breakdown of the starting organometallic compounds. These conditions permitted detection of the activity in the original diphenylmercury and diphenylmercuric hydroxide that indicated occurrence of exchange between these compounds and the solvent (benzene). In these cases the degree of exchange was determined in relation to the original activity after allowing for dilution.

Since diphenyl is formed in the process of breakdown of organometallic compounds, it was necessary to check for the absence of exchange by phenyl radicals between diphenyl and labeled benzene. Investigation of the system diphenyl–benzene under drastic conditions showed that exchange of radicals does not occur. Results of a series of experiments on photolysis and thermal breakdown in the system diphenylmercury–labeled benzene are presented in Table 1.

We see from the data of Table 1 that benzene participates in the photolysis and thermal breakdown of diphenylmercury. Passage of activity into diphenyl is of the order of 20-25%, which is in good agreement with the conclusions of the authors of the paper on the radical character of the reactions cited above.

In formation of an intermediate reaction coil, the activity of the resultant diphenyl should actually be higher due to its uniform distribution between diphenylmercury and benzene. In the event of incomplete

*M. A. Chernyshev and K. I. Vereshchagin participated in the experimental work.

TABLE 1

Photolysis and Thermal Breakdown of Diphenylmercury in Labeled Benzene (Activity of the original benzene 250 pulses/min; volume of counter tube 25 ml; CO_2 pressure 45 mm)

Reaction conditions	Reaction duration (hours)	Activity (pulses/min) of benzene after reaction	Activity (pulses/min) of diphenyl	% exchange
Irradiation with light	50	185	50	20.0
	50	182	51	20.4
	100	196	58	23.2
	100	188	61	24.4
	150	192	60	24.0
	150	189	59	23.8
Heating to 170°	70	195	58	23.2

TABLE 2

Photolysis and Thermal Breakdown of Phenylmercuric Hydroxide in Labeled Benzene (Volume of counter tube 25 ml; CO_2 pressure 45 mm)

Reaction conditions	Reaction duration (hours)	Activity (pulses/min) of original benzene	Activity (pulses/min) of diphenyl	% exchange
Irradiation with light	120	330	150	45.5
	100	568	300	52.8
Heating to 170°	75	568	266	46.8

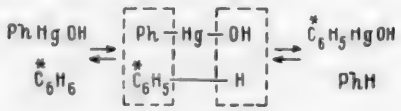
decomposition of the diphenylmercury, a part of the activity appears in the latter. Passage of activity into diphenylmercury is the consequence of the reversibility of the breakdown of diphenylmercury to radicals:

$$PhHg\cdot + C_6^*H_5 \rightleftarrows PhHgC_6^*H_5$$

The maximum transition of activity into diphenylmercury was 10%, but it was usually about 3-4%. Experimental data for the photolysis and thermal breakdown of phenylmercuric hydroxide in benzene are given in Table 2.

As we thus see from Table 2, photolysis and thermal breakdown of phenylmercuric hydroxide results in about 50% of the activity of the benzene passing into the product of breakdown (diphenyl). The presence of considerable activity in phenylmercuric hydroxide was simultaneously detected during its incomplete decomposition. In some experiments this transition of activity was of the order of 23-25%.

It seems to us that the high degree of passage of activity into phenylmercuric hydroxide testifies to formation of a reaction coil whose reversible dissociation leads to transition of activity from the benzene into the hydroxide [1]:



It should be noted that thermal breakdown of phenylmercuric hydroxide results in formation of considerably more insoluble products of decomposition with higher activity than in the case of photolysis.

The same method was employed for the photolysis of tetraphenyllead in benzene solution. The investigations revealed the absence of exchange by phenyl-radicals in this system in the absence of catalysts.

The authors are extremely grateful to G. A. Razuvaev and G. G. Petukhov for their help and counsel.

SUMMARY

1. With the help of carbon-labeled benzene the previously advanced mechanism of photolysis and thermal breakdown of diphenylmercury and phenylmercuric hydroxide was confirmed.

2. It was established that exchange does not occur in the systems diphenyl—benzene and tetraphenyllead—benzene.

LITERATURE CITED

[1] G. A. Razuvaev, G. G. Petukhov, A. F. Rekasheva and G. P. Miklukhin, Proc. Acad. Sci. USSR, 90 569 (1953).

[2] N. D. Zelinskii, Collected Works, Vol. 3, 647 (1955).*

[3] N. P. Keier, B. V. Klimenok and G. V. Isagulianta, Proc. Acad. Sci. USSR, 85, 1029 (1952).

[4] I. A. Korshunov, P. V. Amenitskaia and B. V. Aivazov, Symposium on Application of Labeled Atoms in Analytical Chemistry (in Russian), Acad. Sci. USSR Press (1955), p. 219.

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RADIOCHEMICAL DETERMINATION OF THE NUMBER OF CARBON ATOMS IN AN ORGANIC MOLECULE

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In studies by a number of authors [1-4] internally filled counters have been employed for the determination of activity of compounds containing the radioactive isotope C^{14}. Determination of the activity of labeled compounds is possible when they are directly introduced into the counter tube [4] or in the form of carbon dioxide obtained after combustion of the organic compound in an oxygen stream. Errors of measurement by this procedure do not exceed ± 1%. The high efficiency of the count and the relatively low background value enables counts of low specific activities to be made.

In the present work we demonstrate the possibility of using an internally filled counter for determining the number of carbon atoms in an organic molecule and for determination of the purity of a labeled compound.

We denote by a_g the specific activity of carbon dioxide obtained after combustion of a labeled organic compound (in pulses/min. per mmole); the activity of the labeled compound itself before combustion will be denoted by a_p (pulses/min. per mmole). The ratio a_p/a_g evidently gives the number of carbon atoms in the labeled organic compound corresponding to one radioactive carbon atom in the same compound. The reciprocal ratio a_g/a_p defines the proportion of active carbon atoms (C^{14}) relative to the total number of carbon atoms in the investigated compound.

The specific activity of a specimen is equal to the measured activity of the specimen A and the number of millimoles of compound in the specimen, i.e.:

$$a = A \cdot \frac{RT}{pv}, \qquad (1)$$

where p is the partial pressure of the labeled compound, v is the volume of the counter tube, and T is the temperature (°K).

Since T and v were constant in the experiments, we can write the following expression for the specific activity

$$a = k \cdot \frac{A}{p}, \qquad (2)$$

from which we have:

$$\frac{a_x}{a_g} = \frac{A_x \cdot p_g}{A_g \cdot p_x} \qquad (3)$$

In the presence of a "pure" organic compound and a known number of labeled carbon atoms, equation (3) can be used to find the total number of carbon atoms in the investigated compound from the measured activities at given pressures in the counter tube. But if the composition of the compound is known, then the deviation of the ratio a_p/a_g from the theoretically calculated value enables us to judge the degree of purity of the organic compound.

For a mixture of two pure organic compounds, one of which contains radioactive carbon atoms, the molar proportion of radioactive compound γ is:

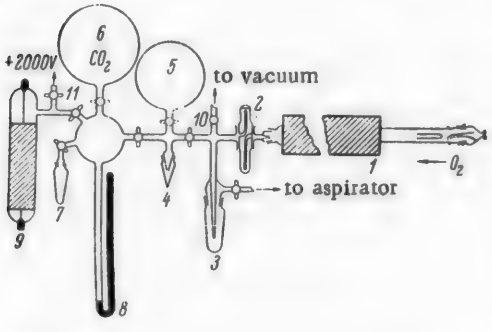
$$\gamma = \frac{a_n}{a_g} \cdot \frac{1}{\nu}, \qquad (4)$$

where ν is the total number of carbon atoms in both of the molecules of the organic compounds.

With the help of the last expression we can find the quantitative composition of a mixture of organic substances.

For our experimental work we synthesized a variety of labeled organic compounds. These included unsaturated hydrocarbons [5] which were prepared by dehydration of labeled alcohols over kaolin catalyst at 400-420°. The olefins were subjected to chromatographic purification. The alcohols [6, 7] were prepared by reduction of esters of 1-C^{14} carboxylic acids with lithium aluminum hydride; alkylbenzenes were prepared by alkylation of benzene with labeled olefins; esters [7] were prepared by esterification of 1-C^{14} carboxylic acids with alcohol; organic acids were prepared by carboxylation with labeled carbon dioxide of organometallic compounds of lithium [8] and magnesium [9].

The radiochemical investigations were conducted in the apparatus illustrated in the drawing. The main component of the counter mixture was carbon dioxide. The organic compound was subjected to microcombustion [10] its activity was measured in the form of $C^{14}O_2$; this combustion was effected in a quartz tube (see drawing). The carbon dioxide was purified with anhydrone in trap 2 and frozen in trap 3 before being transferred to counter tube 9. The background activity was measured with ordinary carbon dioxide prepared from sodium carbonate and sulfuric acid. The CO_2, purified by freezing in traps 2 and 3, was placed in bulb 6. Test tube 7 contained 5-10 ml of anhydrous ethyl alcohol; the alcohol was used as a quenching additive when the tube was charged for determination of the background. Test tube 4 and bulb 5 were filled with volatile organic compounds whose activities had been determined. The manometer 8 was used for proportioning the counter mixture. The accuracy of reading of the pressure was improved with the help of a special cathetometer with a vernier scale graduated in 0.05 mm divisions. Measurements were performed in an AMM-4 type of counter tube 9 with a copper cathode. The working voltage of the tube was 1800-2000 V. The length of the plateau was 200-300 V with a slope of 0.5% per 100 V. The apparatus was connected up at junctions 10 and 11 in vacuo.



Apparatus for radiochemical determination of carbon C^{14}. Explanation in text.

For all of the investigated compounds the length and slope of the plateau of the counter characteristic were determined in dependence on the composition of the mixture; in addition, the relation between the rate of counting and the quantity of labeled substance introduced into the counter was measured, and the reproducibility of the results after a recharge with the same substance was determined.

Measurements were carried out over a period that ensured a statistical error of not more than 1%. The accuracy of determination of the labeled compounds in an internally filled counter was found to be ± 1% for measurements on specimens of carbon dioxide after allowing for the quadratic error and errors in measurements of pressure, etc. In the case of vapors of liquid organic substances the errors increased to 2-10%. The latter depends upon the vapor tension of the compounds introduced into the counter tube. The composition of the counter components, results of measurement of activity of the investigated compounds, and calculations from the formulas are presented in the table.

Results of Measurement of Activity of Labeled Compounds. (Temperature 20°, total pressure in counter tube 60 mm)

Compound investigated	Organic compound: part. pressure in counter mixture (mm)		Organic compound: activity		Carbon dioxide: part. pressure in counter mixture (mm)		Carbon dioxide: activity		Total carbon atoms, labeled molecule	
	p_p of C^{14} compound	CO_2	a_p (pulses/min.)	$a_p \times 10^{-4}$ (pulses/min.) / mmole	ethyl alcohol	p_g of $C^{14}O_2$	A_g (pulses/min.)	$a_p \times 10^{-4}$ (pulses/min.) / mmole	found	calculated
$CH_3C^{14}H_2OH$	14	46	897	2.34	14	46	1451	1.16	2.02	2
$CH_3C^{14}OOCH_3$	14	46	912	2.38	14	46	1022	0.81	2.93	3
$CH_3C^{14}OOC^{14}H_2CH_3$	14	46	988	2.60	14	46	1598	1.28	4.08	4
$CH_3CH_2C^{14}H_2OH$	10	50	806	2.92	14	46	1264	1.00	2.93	3
$CH_3CH_2C^{14}OOCH_3$	15	45	1080	2.63	14	46	820	0.65	4.05	4
$CH_3CH_2C^{14}OOC^{14}H_2CH_3$	15	45	1520	3.69	14	46	1836	1.46	5.08	5
$C^{14}H_2=CH\cdot CH_3$	15	45	3231	7.85	14	46	3340	2.65	2.96	3
$CH_3CH_2CH_2C^{14}OOCH_3$	10	50	1920	7.00	14	46	1738	1.38	5.08	5
$CH_3CH_2CH_2C^{14}OOC^{14}H_2CH_3$	8*	46	1820	8.30	14	46	3556	2.82	5.88	6
	4*	46	1935	17.60	14	46	2898	2.29	7.68	8
	1*	50	1169	43.00	14	46	5480	4.36	9.8	9
$\Sigma C^{14}H_3=CHCH_3$ and $CH_2=CH_2$ (1 : 1)	15	45	1590	3.80	14	46	1878	1.49	2.56	5
$\Sigma CH_3C^{14}H_2OH$ and $CH_3COOC_2H_5$ (1 : 1)	14	46	1278	3.33	14	46	1422	1.13	2.95	6

Our investigations showed that the determination of activity of radioisotope C^{14}-labeled organic compounds possessing a high vapor tension can be performed with great accuracy.

Organic compounds, such as isopropylbenzene and ethylbenzene, which have a low vapor tension, are quantitatively determined with a lower degree of accuracy when directly introduced into the counter tube. An increase in accuracy necessitates preliminary combustion of the compound and conversion into carbon dioxide. The resultant dilution causes the activity per unit of gas pressure in the counter tube to be lowered in proportion to the number of carbon atoms in the burned molecule (Equation 3). The number of carbon atoms in the investigated organic molecules found from these relations and the theoretically calculated values are presented in the Table. The deviation of the experimental values from those calculated, after allowing for experimental errors, permits of quantitative evaluation of the purity of the compounds in question. It follows from the two last experiments that $\gamma = \frac{1}{2}$; consequently the original active vapor undergoes twofold dilution with the inactive component, and this actually occurs.

SUMMARY

1. The possibility was shown of utilizing the internally filled counter for radiometric measurement of active carbon dioxide and of organic compounds with a vapor tension under normal conditions of not less than 4-5 mm mercury column. The labeled compound can be at the same time a quenching additive.

2. Comparison of the activities when counting the labeled C^{14} compound in the form of vapor and carbon dioxide after combustion permits of determination of the total number of carbon atoms in a molecule and of the proportion of isotopic carbon atoms in the same molecule, as well as of quantitative evaluation of the presence of impurities in an organic compound.

LITERATURE CITED

[1] M. Miller, Science 105, 123 (1947).

[2] M. Eidinoff, Science 108, 535 (1948).

[3] J. Labeyrie, J. Phys. rad. 12, 146 (1951).

[4] I. A. Korshunov, R. V. Amenitskaia and B. V. Aivazov, Collected Works on the Application of Labeled Atoms in Analytical Chemistry [in Russian] (Acad. Sci. Press, 1955).

[5] T. I. Andrianova and E. A. Andreev, Proc. Acad. Sci. USSR, 87, 1 (1953).

[6] T. I. Andrianova and E. A. Andreev, Proc. Acad. Sci. USSR, 86, 6 (1952).

[7] T. I. Andrianova and E. A. Andreev, Proc. Acad. Sci. USSR, 86, 5 (1952).

[8] N. F. Novotorov and I. A. Korshunov, J. Gen. Chem. 26, 1959 (1956).*

[9] T. I. Andrianova and E. A. Andreev, Proc. Acad. Sci. USSR, 86, 3 (1952).

[10] M. O. Korshun and N. E. Gel'man, New Methods of Elementary Microanalysis [in Russian] (State Chem. Press, 1949).

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*Original Russian pagination. See C. B. Translation.

THE PROBLEM OF THE DISSOCIATION OF ARYLCARBINOLS AND SOME OTHER COMPOUNDS IN NITROBENZENE. I.

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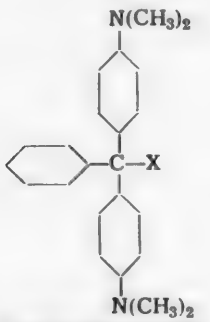
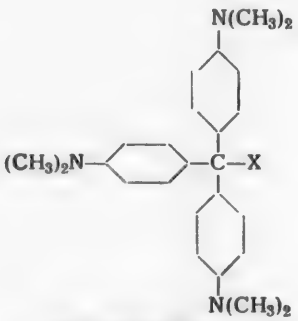
It is well known that in nitrobenzene solutions bis-(p-dimethylaminophenyl)-phenylcarbinol (I) and tris-(p-dimethylaminophenyl)-carbinol (II) slowly undergo progressive dissociation with formation of cations of the dyes Malachite Green and Crystal Violet [1, 2]. Our experiments have shown that similar transformations accompanied by formation of cations of dyes are undergone by the methyl esters of aminotriphenyl carbinols (III and IV) and by the so-called amino bases of triphenylmethane dyes (V and VI) in which the central carbon atom is linked to an amino group.



(I) X=OH; (III) X=OCH$_3$; (V) X=NHC$_6$H$_5$.



(II) X=OH; (IV) X=OCH$_3$; (VI) X=NHC$_6$H$_5$.

With the objective of establishing some physicochemical magnitudes characterizing the state of the above-noted substances in nitrobenzene solutions, we carried out a study of the electrical conductivity and optical density of these solutions. At the same time we investigated nitrobenzene solutions of iodides of Malachite Green (VII) and Crystal Violet (VIII).

Our experiments have shown that in nitrobenzene solutions Malachite Green and Crystal Violet behave like strong electrolytes. On the basis of the data presented in the Experimental part (Table 5), the equivalent electrical conductivities of nitrobenzene solutions of these dyes at infinite dilution were found by graphical extrapolation. The equivalent electrical conductivity at infinite dilution of a nitrobenzene solution of Malachite Green iodide was found to be $\lambda^\circ = 26.5\,\Omega^{-1}$ cm^2, and that of Crystal Violet iodide was $= 25.5\,\Omega^{-1}$ cm^2.

Entirely different relations are observed in a study of the electrical conductivity of nitrobenzene solutions of compounds with a covalent structure. In the first place it should be noted that the electrical conductivity of such nitrobenzene solutions only rises gradually and in the majority of cases it is considerably lower than the conductivity of solutions of dyes of the same concentration. Moreover, dilution of solutions of covalent compounds causes the electrical conductivity to fall disproportionately with the change of concentration. These data, together with the results of a spectrophotometric study of nitrobenzene solutions, show that the slow dissociation that we have studied and which may be represented by the scheme:

increases with dilution. On the basis of the data obtained in spectrophotometric measurements (see Table 8) we succeeded in calculating the degree of dissociation of compounds of the Malachite Green group. The values are given in Table 1.

Starting from the values obtained for the degree of dissociation and the magnitudes of the electrical conductivity of solutions of these compounds (Table 7), it was found possible to calculate the limiting equivalent electrical conductivities of nitrobenzene solutions of compounds (I), (III) and (V); these values are given in Table 1.

TABLE 1

Degree of Dissociation and Limiting Equivalent Electrical Conductivity of Derivatives of Malachite Green

Compound	c (moles/liter)	α (%)	λ°
(I)	$1.6 \cdot 10^{-4}$	21	23.5
(III)	$1.6 \cdot 10^{-4}$	25	23.5
(V)	$8 \cdot 10^{-5}$	57	21

On the basis of the experimental data of Walden [3], we calculated the limiting equivalent electrical conductivity of the iodide ion in nitrobenzene solution and obtained a value of $\lambda^\circ = 20\Omega^{-1}$ cm^2. On the basis of this value and of the values of equivalent electrical conductivity at infinite dilution for Malachite Green iodide, we obtained a value characterizing the limiting equivalent electrical conductivity of cations of Malachite Green in nitrobenzene solutions. This also enabled us to determine the magnitude of the limiting electrical conductivity in nitrobenzene for the OH', OCH_3' and NHC_6H_5' ions. The data so obtained are given in Table 2 (column 2).

Study of nitrobenzene solutions of compounds (II), (IV) and (VI) with a concentration of $1.6 \cdot 10^{-5}$ molar showed that the optical density of such solutions is identical. These data testify to the fact that under the conditions indicated above compounds (II) and (IV) are completely dissociated into cations of the dye and the corresponding anions. An attempt was therefore made to determine the limiting electrical conductivity of compounds (II) and (IV) by the extrapolation method. The same value of $\lambda^\circ = 23.5\Omega^{-1}$ cm^2 was obtained for both of the compounds. Electrical conductivities of the OH' and OCH_3' ions calculated with the help of this value are presented in Table 2 (column 3). We see that the values of limiting electrical conductivity obtained by different methods are in very satisfactory agreement, while the mobilities of OH' and OCH_3' ions are somewhat higher then the mobility of the NHC_6H_5' ion, probably due to the larger volume of the NHC_6H_5' ion in comparison with OH' and OCH_3' ions. At the same time, the data indicate an extremely low mobility of hydroxyl ions in nitrobenzene (nearly 10 times lower than in water); this is evidently due to the mechanism of migration of ions in nitrobenzene being different from the mechanism in aqueous solutions.

Limiting equivalent electrical conductivities of compounds (II), (IV) and (VI) were calculated on the basis of the data of Table 2. The value found for (II) and (IV) was $\lambda^\circ = 23\Omega^{-1}$ cm^2, and that for (VI) was $\lambda^\circ = 20\Omega^{-1}$ cm^2.

The degree of dissociation of the above-described compounds in nitrobenzene solutions was also determined, using the approximation method of Debye and Onsager [4] and the tables of Schedlovsky [5]. The degree of dissociation was calculated from the electtical conductivity values found on the 30th day after preparation of the solutions. Results are presented in Table 3.

TABLE 2

Limiting Electrical Conductivities of Ions in Nitrobenzene Solutions

Ions	From data obtained in a study of compounds of the group (λ°)		Mean value of λ°
	of Malachite green	of Crystal violet	
1	2	3	4
$\left[(CH_3)_2N-C_6H_4\right]_2C^{\cdot}-C_6H_5$	6.5	—	—
OH'	17.0	18.0	17.5
OCH_3'	17.0	18.0	17.5
NHC_6H_5'	14.5	—	—
$\left[(CH_3)_2N-C_6H_4\right]_3C^{\cdot}$	—	5.5	—

TABLE 3

Degree of Dissociation of Some Electrolytes in Nitrobenzene

c (moles/liter)	Degree of dissociation α (%)							
	(VIII)	(II)	(IV)	(VI)	(VII)	(I)	(III)	(V)
$1 \cdot 10^{-2}$	94.1	3.7	6.1	7.1	96.4	1.4	1.1	3.8
$2 \cdot 10^{-3}$	96.2	12.1	27.7	—	97.8	3.5	3.1	8.8
$4 \cdot 10^{-4}$	97.2	51	63.3	75.1	99.7	8.6	9.6	21.5
$8 \cdot 10^{-5}$	98.2	99.2	100	100	100	—	—	—
$1.6 \cdot 10^{-5}$	100	100	100	—	—			

The dissociation constants and the isobaric potentials of formation ΔZ° were calculated for the iodides of Crystal Violet and Malachite Green, as well as for compounds (I), (III) and (V), by extrapolation (with some degree of approximation) by means of the formula of Debye and Onsager [6]. Results appear in Table 4, from which it is evident that compounds (I) and (III) have the same dissociation constants in nitrobenzene and that the constant is only one-tenth of the dissociation constant of compound (V).

It should be noted that the dissociation constant of compounds (II), (IV) and (VI) could not be calculated from the data presented in Table 3. This shows that equilibrium was not attained in all of the solutions that we studied. The probable reason is that in some nitrobenzene solutions these compounds undergo other transformations in addition to dissociation. This theory is supported by our observation of change of color and fall in electrical conductivity in nitrobenzene solutions of compounds (II), (IV) and (VI) with a concentration of $4 \cdot 10^{-4}$ molar and higher after standing for 30 days.

EXPERIMENTAL

The specific electrical conductivity of the nitrobenzene employed as solvent ranged between $1.6 \cdot 10^{-7}$ and $1.8 \cdot 10^{-7}$ Ω^{-1} cm^{-1}.

An amplifier designed according to the data of Luder [7] was included in a standard circuit for measurement of electrical conductivity. Measurements were performed at 25°± 0.05°. The instrument constant K was 0.117. The specific electrical conductivity values in the tables have been corrected for the electrical conductivity of nitrobenzene itself.

TABLE 4

Dissociation Constants and Isobaric Potentials

	Substance				
	(VIII)	(VII)	(I)	(III)	(V)
K	0.1	0.1	$1 \cdot 10^{-6}$	$1 \cdot 10^{-6}$	$1 \cdot 10^{-5}$
$\Delta Z^{\circ}\left(\frac{\text{kcal}}{\text{mole}}\right)$	1360	1360	8200	8200	6800

The SF-11 spectrophotometer was used for the spectrophotometric measurements.

All of the investigated compounds were synthesized according to the literature data [8-12].

Malachite Green (VII) and Crystal Violet (VIII). The electrical conductivity of nitrobenzene solutions of these dyes, taken in the form of iodides [4], remained constant with time. Values are presented in Table 5.

TABLE 5

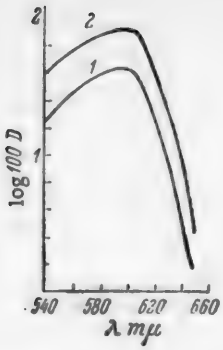
Electrical Conductivity of Nitrobenzene Solutions of Hydriodides of Malachite Green and Crystal Violet

c (moles/liter)	(VII)		(VIII)	
	$\varkappa \cdot 10^{5}$	λ	$\varkappa \cdot 10^{5}$	λ
$1 \cdot 10^{-2}$	20.6	20.6	19.3	19.3
$2 \cdot 10^{-3}$	4.68	23.4	4.42	22.1
$4 \cdot 10^{-4}$	1.01	25.2	0.94	23.6
$8 \cdot 10^{-5}$	0.208	26	0.196	24.5
$1.6 \cdot 10^{-5}$	—	—	0.04	25.0

Tris-(p-dimethylaminophenyl)-carbinol (II), methyl ether of tris-(p-dimethylaminophenyl)-carbinol (IV) and α-anilino-tris-(p-dimethylaminophenyl)-methane (VI). The electrical conductivity of nitrobenzene solutions of these compounds was systematically determined over a period of 30 days from the moment of preparation of the solutions. Results are presented in Table 6.

The absorption spectra of a nitrobenzene solution of compound (II), plotted immediately after preparation and after the lapse of 15 days, are shown in the diagram.

The optical densities of nitrobenzene solutions of compounds (II), (IV), (VI) and (VIII) with a concentration of $1.6 \cdot 10^{-5}$ molar were identical when measured on the 30th day after preparation. After they had been kept for 30 days, the electrical conductivity started to fall and the color started to change in the case of nitrobenzene solutions whose concentrations were $1 \cdot 10^{-2}$, $2 \cdot 10^{-3}$, and $4 \cdot 10^{-3}$ molar. At the same time the electrical conductivity and color of nitrobenzene solutions with concentrations of $8 \cdot 10^{-5}$ and $1.6 \cdot 10^{-5}$ molar remained constant.



Absorption spectra of a nitrobenzene solution of tris-(p-dimethylaminophenyl)-carbinol. 1) immediately after dissolution, 2) 15 days later.

Bis-(p-dimethylaminophenyl)-phenylcarbinol (I), methyl ether of bis-(p-dimethylaminophenyl)-phenylcarbinol (III), α-anilino-bis-(p-dimethylaminophenyl)-phenylmethane (V). Nitrobenzene solution with concentrations of $2 \cdot 10^{-3}$ molar and lower were prepared by successive dilution at intervals of 15 days. Electrical conductivities were measured systematically after 30 days.

Data obtained after 1 hour and on the 30th day after preparation of the solutions are presented in Table 7.

Measurements carried out after several months showed that the electrical conductivity of these solutions no longer changes. At the same time their absorption spectra corresponded to the absorption spectrum of a nitrobenzene solution of Malachite Green hydriodide.

TABLE 6

Electrical Conductivity of Nitrobenzene Solutions of Derivatives of Crystal Violet

C (moles/liter)	Duration (days)	(II)		(IV)		(VI)	
		$\varkappa \cdot 10^8$	λ	$\varkappa \cdot 10^8$	λ	$\varkappa \cdot 10^8$	λ
$1 \cdot 10^{-2}$	1	0.91	0.09	3.35	0.33	4.43	0.44
	2	1.8	0.18	7.25	0.72		
	4	2.77	0.28	10.01	1.0		
	6	3.45	0.35	11.3	1.13		
	8	3.90	0.39	12.2	1.22		
	13	4.95	0.5	12.6	1.26		
	30	8.1	0.8	13.2	1.32	13.32	1.32
$2 \cdot 10^{-3}$	1	0.46	0.23	2.43	1.21	2.55	0.25
	2	1.7	0.85	3.8	1.9		
	4	2.53	1.26	6.1	3.05		
	6	3.25	1.63	7.2	3.6		
	8	3.7	1.85	7.5	3.75		
	13	4.34	2.17	7.8	3.9		
	30	5.36	2.68	12	6		
$4 \cdot 10^{-4}$	1	0.133	0.334	1.8	4.5		
	2	1.51	3.78	2.7	6.75	2.27	5.68
	4	2.25	5.6	3.8	9.5		
	6	2.94	7.35	4.3	10.7		
	8	3.20	8	4.8	12.0		
	13	3.42	8.55	5.3	13.2		
	30	4.54	11.3	7.7	17.5	5.78	14.4
$8 \cdot 10^{-5}$	1	0.03	0.37	1.55	19.3		
	2	0.92	11.5	1.77	22.1	0.54	6.75
	4	1.57	19.6	1.8	22.5		
	6	1.78	22.2	1.8	22.5		
	8	1.79	22.3	1.8	22.5		
	13	1.79	22.3	1.8	22.5		
	30	1.79	22.3	1.8	22.5	1.57	19.6
$1.6 \cdot 10^{-5}$	1				12.5		
	2	0.166	10.44	0.200			
	4	0.35	21.8	0.368	23		
	6	0.364	22.8	0.368	23		
	8	0.364	22.8	0.368	23		
	13	0.364	22.8	0.368	23		
	30	0.364	22.8	0.368	23		

TABLE 7

Electrical Conductivity of Nitrobenzene Solutions of Derivatives of Malachite Green

c (moles/liter)	Duration: A-1 hour B-30 days	(I)		(III)		(V)	
		$\varkappa \cdot 10^6$	λ	$\varkappa \cdot 10^6$	λ	$\varkappa \cdot 10^6$	λ
10^{-2}	A	1.54	0.15	1.23	0.12	2.23	0.22
	B	3.2	0.32	2.7	0.27	7.5	0.75
$2 \cdot 10^{-3}$	A	0.64	0.32	0.68	0.34	2.2	1.1
	B	1.62	0.81	1.44	0.72	3.5	1.8
$4 \cdot 10^{-4}$	A	0.39	0.97	0.42	1.05	1.0	2.5
	B	0.8	2.0	0.89	2.23	1.76	4.4
$1.6 \cdot 10^{-4}$	A	0.25	1.56	0.3	1.88	—	—
	B	0.785	4.9	0.94	5.85	—	—
$8 \cdot 10^{-5}$	A	—	—	—	—	0.43	5.35
	B	—	—	—	—	1.01	12.0

TABLE 8

Optical Density of Nitrobenzene Solutions

Compound	(VII)	(I)	(III)	(V)
c (moles/liter)	$3.2 \cdot 10^{-5}$	$1.6 \cdot 10^{-4}$	$1.6 \cdot 10^{-4}$	$8 \cdot 10^{-5}$
D	1.15	1.21	1.43	1.65

Optical densities for a wave-length of 600 mμ of some nitrobenzene solutions on the 30th day after their preparation are given in Table 8. The layer thickness of the investigated solutions was 4.94 mm.

SUMMARY

1. Iodides of Malachite Green and Crystal Violet behave in nitrobenzene solution like strong electrolytes. On dilution the electrical conductivity changes nearly proportionally to the degree of dilution, and equilibrium is established practically instantaneously.

2. The progressive dissociation of tris-(p-dimethylaminophenyl)-carbinol, methyl ether of tris-(p-dimethylaminophenyl)-carbinol, α-anilino-tris-(p-dimethylaminophenyl)-methane, bis-(p-dimethylaminophenyl)-phenylcarbinol, methyl ether of bis-(p-dimethylaminophenyl)-phenylcarbinol, and α-anilino-bis-(p-dimethylaminophenyl)-phenylmethane increases with the dilution.

3. The degree of dissociation of the above compounds in nitrobenzene solutions was determined at various dilutions. It was found that compounds of the Malachite Green group are less dissociated than the analogous compounds of the Crystal Violet group.

The limiting equivalent electrical conductivities of cations of Malachite Green and Crystal Violet and of OH', OCH_3' and NHC_6H_5' anions were found in nitrobenzene solutions.

5. Dissociation constants and isobaric potentials in nitrobenzene solutions were calculated for the iodides of Crystal Violet and Malachite Green, bis-(p-dimethylaminophenyl)-phenylcarbinol, methyl ether of bis-(p-dimethylaminophenyl)-phenylcarbinol and α-anilino-bis-(p-dimethylaminophenyl)-phenylmethane.

LITERATURE CITED

[1] W. Madelung, J. pr. Ch. (2), 111, 100 (1925).

[2] O. F. Ginzburg, J. Gen. Chem. 23, 1504 (1953). •

[3] P. Walden and E. J. Birr, Z. Phys. Ch. 168, 107 (1934).

[4] S. Glasstone, Introduction to Electrochemistry [Russian translation] (For. Lit. Press, 1951), pp. 133, 223.

[5] R. M. Fuoss and T. Schedlovsky, J. Am. Chem. Soc. 71, 1496 (1949); 73, 4977 (1951).

[6] S. Glasstone, Introduction of Electrochemistry [Russian translation] (For. Lit. Press, 1951), p. 221.

[7] W. F. Luder, J. Am. Chem. Soc. 62, 89 (1940).

[8] O. F. Ginzberg, A. S. Sopova and E. Iu. Shvarts, J. Gen. Chem. Supp. Vol. II, 1100 (1953). •

[9] V. Villiger and E. Kapetschni, Ber. 45, 2910 (1912).

[10] A. Bayer and V. Villiger, Ber. 37, 2867, 2875 (1904).

[11] O. F. Ginzberg, J. Gen. Chem. 23, 1684 (1953). •

[12] V. Villiger and E. Kapetschni, Ber. 45, 2918 (1912).

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INVESTIGATIONS ON CYCLIC ARYLAZO-β-DIKETONES

I. CONDENSATION OF 1,3-INDANDIOL WITH DIAZO COMPOUNDS

Z. Iu. Gudrinietse and G. Ia. Vanag

Compounds containing an active methylene group easily interact with diazo compounds [1, 2]. In continuation of our investigations on cyclic β-diketones, we were interested in their products of interaction with diazo compounds.

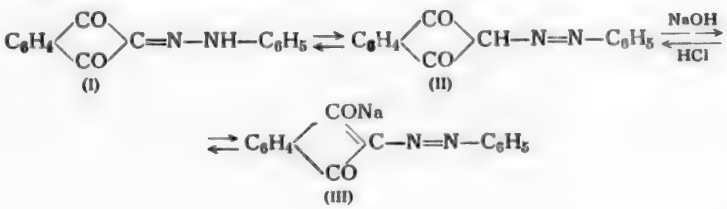
As far back as 1893, Wislicenus and Reitzenstein [3] reacted phenyldiazonium chloride with 1,3-indandione and obtained the β-phenylhydrazone of triketohydrindene (indantrione). Indandione was later condensed with diazotized p-nitroaniline, benzidine, p-toluidine and β-naphthylamine [4]. According to the patent literature [5-7] some indandione azo dyes can be successfully employed for dyeing of fabrics. Derivatives of phenylazoindandione find application in color photography [8]. In our opinion, theoretical and practical importance may be attached to a closer study of these compounds.

In our experiments we coupled 1,3-indandione with various diazotized amines and their derivatives at a pH of 2 to 10. The reaction goes with the highest speed in an alkaline medium, rather more slowly in a neutral medium, and most slowly in an acid medium. Coupling of indandione with diazonium salts in an acid medium is unknown; in fact the literature reports that cyclic β-diketones react only in an alkaline medium, although other compounds containing an active methylene group also react in an acid medium [9, 12].

Products of coupling of indandione with diazo compounds (arylazoindandiones) are yellow to dark-red crystalline substances. They are very poorly soluble in water, ether, chloroform, carbon tetrachloride, gasoline, benzene, toluene and xylene, more soluble in glacial acetic acid, dioxane, acetone and alcohols (the solubility increases with increasing molecular weight of the alcohols), and relatively easily soluble in esters (ethyl acetate, benzyl acetate, methyl and ethyl benzoates). A list of the products that we obtained by coupling indandione with diazotized aromatic amines is given in the Table.

We made a more detailed study of 2-phenylazo-1,3-indandione. The name of this compound may not correspond to its structure, for according to the literature [3] it has the structure of a phenylhydrazone. We still adhere to the opinion that phenylazoindandione exists in two tautomeric forms (I, II) which are in equilibrium; depending upon the conditions, it reacts in the hydrazone (I) or azo (II) form.

Formula (II) is supported by the fact that phenylazoindandione dissolves in caustic alkali and is also slightly soluble in sodium carbonate when heated; it forms enolates (III), acidification of which leads to separation of the original phenylazoindandione (II).



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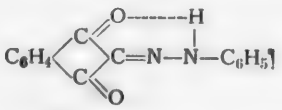
Formula (II) is also supported by the inability of phenylazoindandione to cleave into indandione and phenylhydrazone either by treatment with alkalies or acids. Feofilaktov [10] points out that he also failed to hydrolyze butyrolactone phenylhydrazone. It is possible that the hydrazone form (I) contains a hydrogen bond which renders this form (IV) resistant to hydrolytic agents.



(IV)

Bromination of phenylazoindandione gives p-bromophenylazoindandione, which is also obtained on coupling indandione with diazotized p-bromoaniline. Sulfonation of phenylazoindandione gives p-sulfophenylazoindandione, which is also obtained by coupling of indandione with diazotized sulfanilic acid. It has good solubility in water and is isolated as the sodium salt. It imparts a bright-yellow color to wool and natural silk.

Nitration of phenylazoindandione gave p-nitrophenylazoindandione, which is identical with the product from indandione and diazotized p-nitroaniline. It is photosensitive and changes in color from yellow to greenish-brown.

The corresponding carbonyl group derivatives are formed by phenylazoindandione with phenylhydrazine, hydrazine and hydroxylamine. Reduction of phenylazoindandione gives various products (depending on the reaction conditions) whose examination is in progress.

EXPERIMENTAL

2-Phenylazo-1,3-indandione (I, II). 6.6 g of aniline in 18 ml of concentrated hydrochloric acid, diluted with 36 ml of water, was diazotized with 5.8 g of sodium nitrite. With constant stirring, the diazotized solution was run into a cooled solution of 10.3 g of indandione in sodium hydroxide solution. The mixed solution should have a pH of 7-9; more alkali can be added if needed. The liquid is left in a freezing mixture with constant stirring for 1.5-2 hr. and then acidified and suction-filtered. The product is crystallized from methanol or ethanol or their mixtures with glacial acetic acid, or from methyl or ethyl benzoate or benzyl acetate. The purest product and the highest yields are obtained from methanol or ethanol (10 g of crude product is dissolved with boiling in 700 ml of ethanol). The yield of 2-phenylazo-1,3-indandione is 12 g (68%); orange needles; m. p. 192-193° (the literature reports 190°). Insoluble in water and ether, poorly soluble in acetone, benzene and its homologs, better soluble in glacial acetic acid, alcohols and esters.

Found %: N 11.32. $C_{15}H_{10}O_2N_2$. Calculated %: N 11.20.

Other arylazoindandiones are similarly obtained by diazotization of other aromatic amines and coupling with indandione (see Table).

p-Bromophenylazoindandione. Bromine was added to 2.5 g of phenylazoindandione in 30 ml of glacial acetic acid and the mass was held at room temperature for 12-14 hours. The orange, crystalline precipitate was recrystallized from benzene. Yield 2.4 g (73%), m. p. 245°. Bromine is not split off on boiling with alkali.

Found %: N 8.53. $C_{15}H_9O_2N_2Br$. Calculated %: N 8.51.

The same p-bromophenylazoindandione was obtained by coupling indandione with diazotized p-bromoaniline in an alkaline medium. M. p. 243-245°; a mixture with the preceding preparation melts without depression.

Found %: N 8.85. $C_{15}H_9O_2N_2Br$. Calculated %: N 8.51.

2-Arylazo-1,3-indandiones C_6H_4(CO)(CO)$CH-N=N-Ar$

Preparation No.	Diazotized amine	Ar	Recrystallized from	Melting point	Color	Empirical formula	Nitrogen content (%) found	Nitrogen content (%) calc.
1	Aniline	C_6H_5	Ethanol	192—193°	Orange	$C_{15}H_{10}O_2N_2$	11.32	11.20
2	o-Nitroaniline	o-$C_6H_4NO_2$	Glacial acetic acid	290—292	Yellow	$C_{15}H_9O_4N_3$	14.37	14.23
3	m-Nitroaniline	m-$C_6H_4NO_2$	Dioxane	301—303	Yellow	$C_{15}H_9O_4N_3$	14.01	14.23
4	p-Nitroaniline	p-$C_6H_4NO_2$		311—313	Brownish	$C_{15}H_9O_4N_3$	14.48	14.23
5	p-Bromoaniline	p-C_6H_4Br	Benzene	243—245	Yellow	$C_{15}H_9O_2N_2Br$	8.85	8.51
6	o-Aminophenol	o-C_6H_4OH	Alcohol	250—252	Brownish	$C_{15}H_{10}O_3N_2$	10.56	10.52
7	m-Aminophenol	m-C_6H_4OH	Alcohol	273—274	Brown	$C_{15}H_{10}O_3N_2$	10.70	10.52
8	p-Aminophenol	o-C_6H_4OH	Alcohol	248—249	Red-brown	$C_{15}H_{10}O_3N_2$	10.85	10.52
9	o-Toluidine	o-$C_6H_4CH_3$	Alcohol	193—195	Orange	$C_{16}H_{12}O_2N_2$	10.81	
10	m-Toluidine	p-$C_6H_4CH_3$	Alcohol	185	Red	$C_{16}H_{12}O_2N_2$	10.68	10.60
11	p-Toluidine	m-$C_6H_4CH_3$	Alcohol	203	Brownish	$C_{16}H_{12}O_2N_2$	10.60	10.60
12	α-Naphthylamine	α-$C_{10}H_7$	Benzyl acetate	232	Red	$C_{19}H_{12}O_2N_2$	9.47	9.33
13	β-Naphthylamine	β-$C_{10}H_7$	Benzyl acetate	242	Orange	$C_{19}H_{12}O_2N_2$	9.63	9.33
14	p-Aminoazobenzene	p-$C_6H_4-N=N-C_6H_4$	Pyridine	273—274	Red	$C_{21}H_{14}O_2N_4$	15.36	15.81
15	Anthranilic acid	o-C_6H_4COOH	Alcohol	—	Brownish	$C_{16}H_{10}O_4N_2$	8.81	9.52
16	m-Aminobenzoic acid	m-C_6H_4COOH	Alcohol	—	Yellow	$C_{16}H_{10}O_4N_2$	9.36	9.52
17	p-Aminobenzoic acid	p-C_6H_4COOH	Alcohol	—	Brownish	$C_{16}H_{10}O_4N_2$	—	—
18	Sulfanilic acid	p-$C_6H_4SO_3H$	Water (sodium salt)	—	Yellow	$C_{15}H_9O_5N_2SNa$	7.52	7.98

Sodium p-(indandionylazo)-benzenesulfonate. 0.5 g of phenylazoindandione and 5 ml of concentrated sulfuric acid were heated for 10-15 min. at 60°. The red solution turned yellow after dilution with water. The solution was saturated with sodium chloride. The sodium salt of indandionylazo-p-benzenesulfonic acid came down. Soluble in water and alcohol. It was purified by crystallization from water. In aqueous or acetic acid solution it colors wool and natural silk bright-yellow. The same product was obtained by coupling indandione with diazotized sulfanilic acid.

Found %: N 7.52, 7.45; Na 6.31. $C_{15}H_9O_5N_2SNa$. Calculated %: N 7.90; Na 6.51.

p-Nitrophenylazoindandione. 0.5 g of phenylazoindandione, 3 ml of glacial acetic acid and 3 ml of concentrated nitric acid were heated to 60-70°. The phenylazoindandione dissolved but a yellow precipitate came down at once. Crystallization from glacial acetic acid gave 0.2 g of yellow, finely crystalline p-nitrophenylazoindandione. M. p. 273°. Insoluble in water and ether, poorly soluble in alcohol and aromatic hydrocarbons; readily soluble in pyridine.

Found %: N 13.80, 14.63. $C_{15}H_9O_4N_3$. Calculated %: N 14.23.

The same p-nitrophenylazoindandione was prepared by coupling indandione with diazotized p-nitroaniline.

Phenylazoindandione monoxime. Five g of phenylazoindandione, 2.1 g of hydroxylamine hydrochloride and 100 ml of ethanol were boiled on a water bath for 1.5-2 hrs. The orange, finely crystalline precipitate was crystallized from dioxane. Yield of phenylazoindandione monoxime 5.2 g (98%). Yellow needles, m. p. 256-257°; m. p. 264-265° after crystallization from benzyl acetate.

Found %: N 15.78. $C_{15}H_{11}O_2N_3$. Calculated %: N 15.85.

Phenylazoindandione monophenylhydrazone. 1.25 g of phenylazoindandione, 2.16 g of phenylhydrazine and 70 ml of ethanol were boiled. The liquid turned red. Red crystals came down after 20 minutes. The mass was boiled for another 15 minutes. Crystallization from glacial acetic acid gave matted crystals with m. p. 241°.

Found %: N 16.92. $C_{21}H_{16}ON_4$. Calculated %: N 16.47.

Phenylazoindandione azine. 1.25 g of phenylazoindandione, 2.6 g of hydrazine sulfate, 1.64 g of anhydrous sodium acetate and 50 ml of ethanol were boiled for 2 hours. After cooling, the mass was poured into a 4-fold amount of water, and the precipitate was crystallized from ethanol. Dark-red needles of phenylazoindandione azine; m. p. 225-228°.

Found %: N 17.28. $C_{20}H_{20}O_2N_6$. Calculated %: N 16.93.

SUMMARY

1. Optimum conditions were established for the preparation of 2-phenylazo-1,3-indandione, a series of other 2-arylazo-1,3-indandiones were also synthesized.

2. A series of derivatives of 2-phenylazo-1,3-indandione were prepared: p-bromophenylazoindandione, p-nitrophenylazoindandione, p-sulfophenylazoindandione, phenylazoindandione monoxime, phenylazoindandione phenylhydrazone and azine.

LITERATURE CITED

[1] K. H. Saundlers, The Aromatic Diazo-Compounds and Their Technical Applications, London, 209 (1947).

[2] K. Holzach, The Aromatic Diazo Compounds [In German] (Stuttgart, 1947), p. 151.

[3] W. Wislicenus and F. Reitzenstein, Lieb. Ann. 277, 362 (1893).

[4] A. Das. B. N. Ghosh, J. Am. Chem. Soc. 43, 1739 (1921).

[5] German Patent, 241723; Zbl., 1912, I, 179.

[6] German Patent, 241630; Zbl., 1912; I, 178.

[7] French Patent, 640746; Zbl., 1928, II, 2064.

[8] Canad. Patent, 436212, Ch. A., 1946, 6352.

[9] S. Hünig and O. Boes, Lieb. Ann. 579, 28 (1953).

[10] V. V. Feofilaktov and A. S. Onishchenko, J. Gen. Chem. 9, 318 (1939).

[11] C. Bülow, Lieb. Ann. 236, 194 (1886).

[12] C. Bülow and F. Schlotterbeck, Ber. 35, 2187 (1902).

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INVESTIGATIONS ON IMIDAZOLE DERIVATIVES

XVIII. THE PROBLEM OF THE NITRATION OF 5-METHYLBENZIMIDAZOLE*

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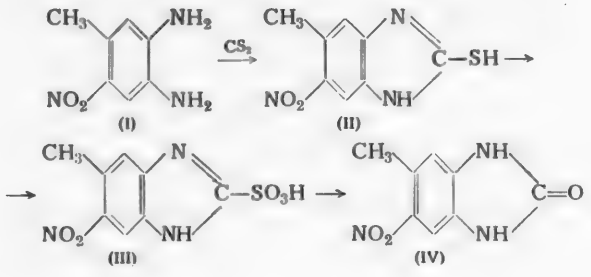
In a study of the chemical properties of derivatives of benzimidazole, we needed to prepare 5-methyl-6-nitrobenzimidazolone (IV) with precisely known location of the substituents. In this connection we carried out partial reduction of 2,4-dinitro-5-methylaniline. We obtained, however, a mixture of products from which it was fairly difficult to isolate the individual amines. Fusion of the mixture with urea leads to a still more impure product.

For the synthesis of substance (IV), we therefore decided to use an indirect route. Treatment of a mixture of the amines with carbon disulfide in a medium of alcoholic potassium hydroxide gave 5-methyl-6-nitro-2-mercaptobenzimidazole (II) which was very easily oxidized by permanganate in an alkaline medium to give the sulfoacid (III) which was hydrolyzed by hydrochloric acid to our required benzimidazolone derivative (IV).



For the purpose of identification of the starting 1,2-diamino-4-methyl-5-nitrobenzene (I), we decided to prepare from it the 2,5-dimethyl-6-nitrobenzimidazole (XI) previously described by Niementowski [1, 2]. On heating a mixture of the products of partial reduction of 2,4-dinitro-5-methylaniline with acetic anhydride, we obtained a substance that was found to be identical with the product of nitration of 2,5-dimethylbenzimidazole by Niementowski's method [1, 2].

By boiling our mixture of products of partial reduction of 2,4-dinitro-5-methylaniline with formic acid, we obtained a 65% yield of a substance melting at 197° and corresponding in empirical composition with methylnitrobenzimidazole. This compound must of course be 5-methyl-6-nitrobenzimidazole (X).

A melting point of 241° is given, however, in a paper by O. Fischer and W. Hess [3] for a product of the same structure synthesized by nitration of 5-methylbenzimidazole (V). Such a large difference in the melting points of the two preparations prompted us to repeat the experiments of O. Fischer and W. Hess [3] on the nitration of 5-methylbenzimidazole.

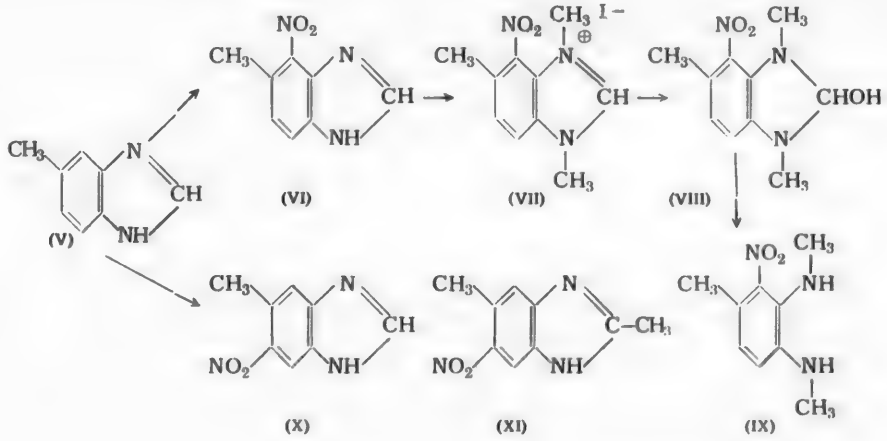
*Preceding communication: J. Gen. Chem. 27, 684 (1957).

On carrying out this reaction in concentrated sulfuric acid with theoretical quantity of nitric acid, we obtained a 75-80% yield of a product melting gradually at 180-220°. After 2 crystallizations from alcohol, we isolated a substance relatively sparingly soluble in alcohol and melting at 240°. The mother liquors from the purification yielded a compound very easily soluble in alcohol, identical with the 5-methyl-6-nitrobenzimidazole (X) that we had synthesized with m. p. 197°. The product with m. p. 240° also had the empirical composition of a methylnitrobenzimidazole and could only be the 5-methyl-4-nitro isomer (VI) since the third possible structural isomer – 5-methyl-7-nitrobenzimidazole – that we synthesized was very unlikely to be formed in the present case and had m. p. 289.5°.

O. Fischer and W. Hess based their assignment of the structure of the product with m. p. 241° on the transformation of this compound into di-(methylamino)-nitromethylbenzene with m. p. 194° by exhaustive methylation with methyl iodide and opening of the dihydroimidazole ring with alkali. They synthesized the same product by a similar route from 2,5-dimethyl-6-nitrobenzimidazole• obtained by them according to Niementowski's method [1, 2].

We also repeated this part of the work of Fischer and Hess [3]. From the substance with m. p. 240°, to which (as noted below) we must assign the structure of 5-methyl-4-nitrobenzimidazole (VI), we obtained the methoiodide of 1,5-dimethyl-4-nitrobenzimidazole (VII) with m. p. 212°, and from the latter we prepared 1,3,5-trimethyl-4-nitro-2-hydroxydihydrobenzimidazole (VIII) with m. p. 169°; finally, from the latter we obtained 1,2-di-(methylamino)-3-nitro-4-methylbenzene (IX) which melted at 30-31° and distilled without decomposition at 140° (3 mm). In the paper under comparison the respective melting points were 238, 150 and 194°.

It must be assumed that when they nitrated 5-methylbenzimidazole, Fischer and Hess did not observe the formation of two reaction products and performed all the transformations described above with their mixture; their end product was therefore evidently a mixture of ortho-diamines, of which 1,2-di-(methylamino)-3-nitro-4-methylbenzene, as we showed, is very low-melting and is distinguished by high solubility in organic solvents. It could be isolated with facility by recrystallization, and this circumstance enabled the authors in question to isolate 1,2-di-(methylamino)-4-methyl-5-nitrobenzene with m. p. 194° according to their data.



Having established that nitration of 5-methylbenzimidazole gives two isomeric nitro products, we attempted to evaluate their ratio. With this objective [4] we plotted the ultraviolet absorption spectra in ethanol of 5-methyl-6-nitrobenzimidazole (X) and 5-methyl-4-nitrobenzimidazole (VI), as well as of their mixture prepared in 75-80% yield by nitration (Fig. 1).••

• An error evidently crept into the paper of Fischer and Hess [3]. The authors write that for 2,5-dimethyl-6-nitrobenzimidazole "in agreement with Niementowski m. p. 210° was found," whereas an m. p. of 201° is both by Niementowski [1] and by Maron and Salzberg [2] who repeated the work.

•• The spectra were plotted with a Russian SF-4 spectrophotometer using quartz cells with a layer thickness of 1 cm (ethyl alcohol) and 0.5 cm (hydrochloric acid) at concentrations of respectively $3.9\text{-}3.6 \cdot 10^{-5}$ and $6.9 \cdot 10^{-5}$ mole/liter.

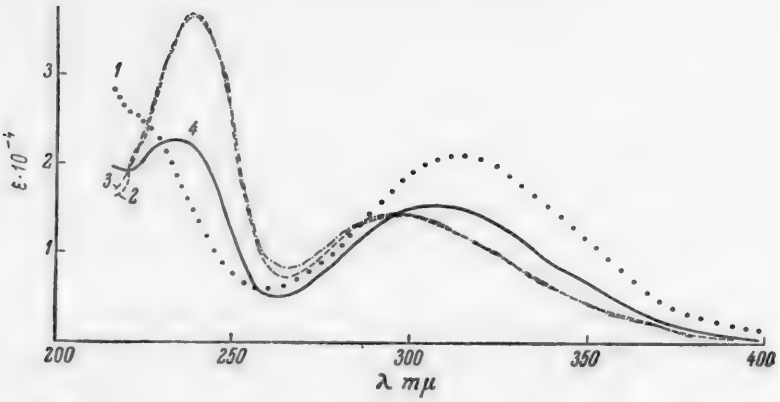


Fig. 1. Ultraviolet absorption spectra in ethyl alcohol. 1) 5-methyl-4-nitrobenzimidazole; 2) 5-methyl-6-nitrobenzimidazole; 3) 5-methyl-6-nitrobenzimidazole isolated from products of nitration of 5-methylbenzimidazole; 4) mixture of products of nitration of 5-methylbenzimidazole.

The mixture of isomers absorbed less intensively in the wavelength ranges of 220-230 mμ and 257-296 mμ than each of the components separately. Calculation on this basis gave a negative percentage content of isomers in the mixture and did not permit of any trustworthy calculations at other wavelengths. Reaction in solution of two amphoteric substances with different basicities was evidently involved [5]. This prompted us to study the absorption spectra of the investigated compounds in an acid medium whose pH was so low that hydrolysis of the salts was completely suppressed. As the solvent we selected 0.5% solution of hydrochloric acid, and we obtained the transmission curves plotted in Fig. 2.

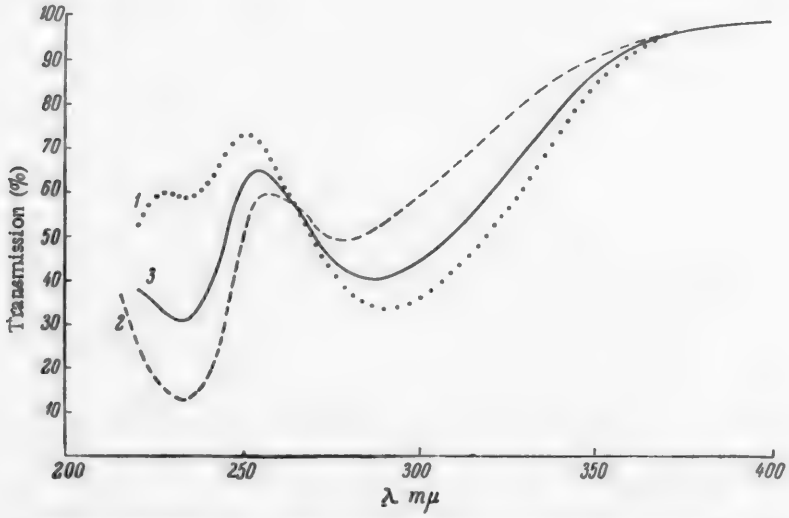


Fig. 2. Ultraviolet absorption spectra in 0.5% aqueous hydrochloric acid. 1) 5-methyl-4-nitrobenzimidazole; 2) 5-methyl-6-nitrobenzimidazole; 3) mixture of products of nitration of 5-methylbenzimidazole.

Wavelength (mμ)	5-Methyl-6-nitrobenzimidazole (%)	5-Methyl-4-nitrobenzimidazole (%)
232	42.7	57.3
290	43.6	56.4
300	43.2	56.8
Mean	43.1	56.9

Results of the calculations carried out for appropriate points [4] are presented in the Table.

Consequently, the nitration of 5-methylbenzimidazole gives a mixture of 4- and 6-nitro derivatives in the ratio of 5.7 : 4.3.

EXPERIMENTAL

Reduction of 2,4-dinitro-5-methylaniline. 23.7 g of 2,4-dinitro-5-methylaniline [6], 250 ml of ethyl alcohol, 50 ml of pyridine and 100 ml of concentrated aqueous ammonia were put into a flask fitted with a stirrer, a reflux condenser and a gas-leading tube extending to the bottom of the flask. With intensive stirring, a strong stream of hydrogen sulfide was passed through until the precipitate had completely dissolved (30-40 minutes). The heater was then removed and hydrogen sulfide was passed through for a further 20 minutes. The reaction mass was evaporated to dryness in vacuo and the dry residue was treated with three portions of a boiling mixture each comprising 90 ml of water and 10 ml of conc. hydrochloric acid. The extracts obtained were combined and heated with active carbon; after filtration from carbon and impurities, the liquid was cooled. Neutralization of the strongly colored solution with ammonia brought down dark-red crystals which weighed 12 g after drying and did not melt sharply at 126-129°.

5-Methyl-6-nitro-2-mercaptobenzimidazole (II). 6.4 g of diamine with m. p. 126-129°, 5 ml of hydrogen sulfide, 65 ml of alcohol and 4.2 g of potassium hydroxide were heated for 3 hours on a water bath in a flask connected with a reflux condenser. Seven ml of glacial acetic acid was then added and the solution was evaporated to dryness in vacuo. The dry residue was treated with 200 ml of boiling aqueous 2.5% solution of sodium hydroxide with addition of a few drops of aqueous sodium bisulfite solution. Treatment with active carbon scarcely decolorized the solution but facilitated filtration of the alkali-insoluble impurities. The cold mother liquor was neutralized with concentrated hydrochloric acid until neutral to Congo. After filtration, the precipitate was twice recrystallized from alcohol. An amorphous, easily electrified powder with a yellow color, melting at 284.5° (decomp.). Yield 3.5 g.

Found %: S 15.29, 15.02. $C_8H_7N_3O_2S$. Calculated %: S 15.33.

5-Methyl-6-nitrobenzimidazolone (IV). To a solution of 3.5 g of 5-methyl-6-nitro-2-mercaptobenzimidazole (II) and 1 g of sodium hydroxide in 25 ml of water was added (with stirring) a cold saturated solution of 2.65 g of potassium permanganate in water at such a rate that the temperature did not rise above 35°. Another 2.65 g of pulverized permanganate was then added, after which the manganese dioxide was filtered off and washed with water. The small excess of permanganate in the filtrate was removed with sodium bisulfite, the solution (volume about 100 ml) was neutralized with concentrated hydrochloric acid until acid to Congo and concentrated to a volume of 30 ml. A yellowish precipitate appeared during the evaporation. The suspension was diluted with 20 ml of concentrated hydrochloric acid and heated in sealed tubes for 3 hours at 120°. A strong odor of sulfur dioxide was detected when the tubes were opened. The precipitate was filtered, twice reprecipitated from alkali with acid and recrystallized from glacial acetic acid. Two g of 5-methyl-6-nitrobenzimidazolone (IV) was obtained in the form of faint-yellowish, fine needles with m. p. 325° (decomp.). The compound is sparingly soluble in organic solvents.

Found %: N 21.81, 21.71. $C_8H_7O_3N_3$. Calculated %: N 21.75.

5-Methyl-6-nitrobenzimidazole (X). A solution of 1 g of diamine with m. p. 126-129° in 10 ml of 100% formic acid was refluxed in a flask for 2 hours. 2.5 ml of concentrated hydrochloric acid was then added and the solution was evaporated to dryness in a dish on a water bath. The dry precipitate was dissolved in 20 ml of boiling water and treated with animal charcoal. After the charcoal had been filtered off, the cold mother liquor was acidified with excess of nitric acid. The precipitated nitrate of 5-methyl-6-nitrobenzimidazole

was dissolved in 20 ml of boiling water and treated with animal charcoal; the resultant faintly colored solution was neutralized with ammonia. The precipitate was recrystallized 3 times from 50% aqueous alcohol. Slightly yellowish, very slender needles, easily soluble in alcohol, sparingly soluble in water; m. p. 197°. Yield 65%, reckoned on the diamine.

Found %: C 54.09, 54.01; H 4.03, 4.21. $C_8H_7O_2N_3$. Calculated %: C 54.24; H 3.98.

2,5-Dimethyl-6-nitrobenzimidazole (XI). A solution of 1 g of diamine with m. p. 126-129° in 10 ml of acetic anhydride was refluxed in a flask for 1 hour; 2.5 ml of concentrated hydrochloric acid was then added, and the solution was heated for another hour and evaporated to dryness in a dish on a water bath. The dry residue was dissolved in 20 ml of boiling water and treated with carbon; the filtrate was neutralized with ammonia. The precipitate was recrystallized 3 times from water and once from aqueous alcohol. The slightly yellowish powder, dried at 120°, melted at 200-201°. The product did not show a depression of melting point when mixed with the compound prepared by nitration of 2,5-dimethylbenzimidazole by Niementowski's method [1, 2].

5-Methyl-7-nitrobenzimidazole. 0.7 g of 1,2-diamino-3-nitro-5-methylbenzene [7] (m. p. 158°) and 6 ml of 100% formic acid were refluxed for 2 hours in a flask. Two ml of concentrated hydrochloric acid was then added, and the reaction mass was evaporated to dryness in a dish on a water bath. The dry residue was dissolved in 30 ml of boiling water and treated with carbon; the light-yellow solution was neutralized with ammonia. The precipitate was recrystallized twice from methanol. 5-Methyl-7-nitrobenzimidazole forms long, silky, nearly colorless needles with m. p. 289.5°, sparingly soluble in water and cold alcohol. Yield 70%.

Found %: C 54.33, 53.95; H 4.27, 4.01. $C_8H_7O_2N_3$. Calculated %: C 54.24; H 3.98.

5-Methylbenzimidazole (V). 5-Methylbenzimidazole was synthesized from 1,2-diamino-4-methylbenzene prepared, analogously to o-phenylenediamine [8], from 3-nitro-4-aminotoluene with the slight modification that the diamine was not isolated but the alcoholic solution containing the diamine was evaporated nearly to dryness in vacuo; the wet slurry was treated with a considerable excess of 85% formic acid and refluxed in a flask for 2 hours. Carbon was carefully added to the flask 20 minutes before the end of the reaction; the carbon was then filtered off and washed on the filter with a small quantity of warm water which was added to the reaction mass. The deeply colored solution was evaporated to dryness in a dish on a water bath; the dry residue was dissolved in water (800 ml for 0.5 mole of initial nitrotoluidine), and the cold solution was cautiously neutralized with ammonia with stirring. The precipitated product, which was badly contaminated at the start, was separated by filtration and centrifuged. The main bulk of 5-methylbenzimidazole came down in the form of a dark oil which was separated from the water and distilled in vacuo. 5-Methylbenzimidazole distilled without decomposition at 173° (3 mm) and set to a gummy, light-yellow mass. Yield 75% reckoned on the nitrotoluidine.

Nitration of 5-methylbenzimidazole. To a solution of 47 g of 5-methylbenzimidazole (V) in 185 ml of concentrated sulfuric acid was added 15 ml of nitric acid (d 1.5) at 0° with stirring. The reaction mass was stirred for 1 hour without cooling, the temperature rising to 20°. The yellow solution (about 900 ml) was poured on to ice; excess of nitric acid was then added. The precipitate was filtered off, well pressed,* and dissolved in the minimum quantity of boiling water; it was then precipitated from the hot solution with ammonia. Yield 75-80%. Crystallization from 1200 ml of alcohol gave 22.4 g of substance melting (after recrystallization) at 240°. The melting point of the 5-methyl-4-nitrobenzimidazole (VI) remained unchanged after further purification. The product is sparingly soluble in cold alcohol, almost insoluble in water.

Found %: C 53.96, 54.14; H 3.35, 3.60. $C_8H_7O_2N_3$. Calculated %: C 54.24; H 3.98.

Nearly complete evaporation of the alcoholic mother liquors after crystallization of the product described above led to separation of a substance melting at 167-187°.** Numerous recrystallizations from a small volume of alcohol enabled separation of a very small quantity of substance with m. p. 196°, easily soluble in alcohol. Judging by the absorption spectrum (Fig. 1), the crystal form, and the solubility, the compound is identical with 5-methyl-6-nitrobenzimidazole (X); a mixture with the latter melted at 196.5°.

*A very small quantity of substance, which was not investigated, came out of the mother liquor on neutralization with ammonia.

**As in original – Publisher's note.

Methoiodide and methoperiodide of 1,5-dimethyl-4-nitrobenzimidazole. Four g of 5-methyl-4-nitrobenzimidazole (VI), 20 ml of methanol and 2.9 ml of methyl iodide were heated in a sealed tube for 5 hours at 140-150°. The precipitate was treated on the filter with three portions of 15 ml each of methanol and recrystallized from methanol. Rapid cooling resulted in deposition of light, thin, dark-red crystals of the periodide, melting at 114°. 0.6 g of the methoperiodide of 1,5-dimethyl-4-nitrobenzimidazole was obtained.

Found %: I 65.30, 64.98. $C_{10}H_{12}O_2N_3I_3$. Calculated %: I 64.87.

The methanol solution obtained on washing of the periodide was combined with the main filtrate and diluted with twice the volume of ether. The precipitate of methoiodide consisted of heavy, light-yellow needles with m. p. 212° (from alcohol). 3.5 g of 1,5-dimethyl-4-nitrobenzimidazole methoiodide (VII) was obtained.

Found %: C 36.19; H 3.07; I 38.32, 38.07. $C_{10}H_{12}O_2N_3I$. Calculated %: C 36.05; H 3.63; I 38.10.

1,3,5-Trimethyl-4-nitro-2-hydroxydihydrobenzimidazole (VIII). 4.5 g of 1,4-dimethyl-4-nitrobenzimidazole (VII) was dissolved in 50 ml of water, and an excess of 20% sodium hydroxide solution was added to the solution. A red oil separated out at once and rapidly crystallized and turned yellow. The precipitate was filtered off and recrystallized from aqueous alcohol containing active carbon. 2.3 g of a bright-yellow finely crystalline powder was obtained; m. p. 169°.

Found %: C 53.63, 53.55; H 5.87, 6.03. $C_{10}H_{13}O_3N_3$. Calculated %: C 53.80; H 5.87.

The same carbinol can be obtained by dropwise addition of an excess of aqueous bisulfite solution to a warm methanol solution or suspension of the periodide, slight dilution of the faintly yellowish solution with water, and precipitation of the product with alkali.

1,2-Di-(methylamino)-3-nitro-4-methylbenzene (IX). A mixture of 3.5 g of the above-described carbinol (VIII), 50 ml of water and 20 g of sodium hydroxide was distilled in steam until a red oil ceased to distill over (volume of liquid about 1 liter). The distillate was extracted with 4 portions of 30 ml each of chloroform, and the chloroform extracts were combined, washed with 40 ml of water and evaporated. The residue was distilled in vacuo: 1,2-di-(methylamino)-3-nitro-4-methylbenzene (IX) came over at 140° (3 mm). A fairly mobile liquid with a red color, rapidly crystallizing in the cold to light-red crystals melting at 30-31°. The product dissolves very easily in organic solvents and sparingly in water. Yield 2 g.

Found %: C 55.63, 55.40; H 6.69, 6.67. $C_9H_{13}O_2N_3$. Calculated %: C 55.32; H 6.72.

SUMMARY

1. Nitration of 5-methylbenzimidazole gives the 4- and 6-mononitro derivatives in the ratio of 5.7:4.3.

2. It was established that the product with m. p. 240° is 5-methyl-4-nitrobenzimidazole and not the 6-nitro derivative as claimed by O. Fischer and W. Hess.

LITERATURE CITED

[1] St. Niementowski, Ber. 19, 724 (1886).

[2] D. Maron and D. Salzberg, Ber. 44, 3002 (1911).

[3] O. Fischer and W. Hess, Ber. 36, 397 (1903).

[4] M. Barnard and P. Mc. Michael, Ind. Eng. Ch. (Anal. Ed.) 2, 363 (1930).

[5] L. S. Efros and B. A. Porai-Koshits, J. Gen. Chem. 23, 697 (1953).*

[6] W. Borshe and A. Fiedler, Ber. 46, 2127 (1913).

*Original Russian pagination. See C. B. Translation.

[7] H. Lindemann and H. Krause, J. pr. Ch. 115, 265 (1927).

[8] Synthetic Organic Preparations [Russian translation] 2, 509 (1949).

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THE CONDENSATION OF METHYL ESTERS OF α-AMINO-β-MERCAPTOCARBOXYLIC ACIDS WITH BROMOPYRUVIC ACID

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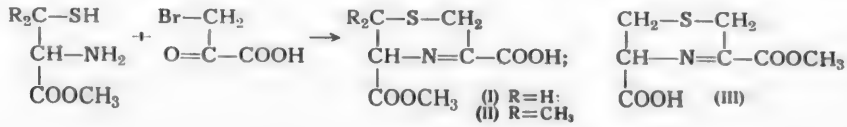
Condensation of methyl esters of L-cysteine and DL-penicillamine with bromopyruvic acid in a chloroform medium and in presence of triethylamine gave yellow crystalline substances (I) and (II) containing one free and one esterified carboxyl group. Judging by the analysis, they are derivatives of the 5,6-dihydrothiazine series whose double bond is evidently (in view of the course of the synthesis) in the 3,4-position.



(I) R=H; (II) R=CH$_3$ (III)

Conclusive proof of the structure of these compounds has not yet been obtained since the possibility of migration of the double bond into the 2,3-position is not excluded.

Compounds (I) and (II) readily lose the carboxyl group on heating above 100°.

Condensation of cysteine hydrochloride with methyl bromopyruvate gave cystine hydrochloride and 5,6-dihydro-3-carbomethoxy-$\Delta^{3,4}$-thiazin-5-carboxylic acid (III).

The bromine in methyl bromopyruvate evidently possesses a positive charge and is capable of oxidizing sulfide groups.

EXPERIMENTAL

5,6-Dihydro-5-carbomethoxy-$\Delta^{3,4}$-thiazin-3-carboxylic acid. Into a 50 ml round-bottomed flask were placed 3 g of the hydrochloride of the methyl ester of L-cysteine, 2.9 g of bromopyruvic acid [1] and 30 ml of anhydrous chloroform; 7 ml of triethylamine was then added gradually with stirring and cooling. The solid material went into solution and the latter gradually acquired an orange-yellow color. The following day, the reaction mass was washed with 5 ml of water and 10 ml of 2 N hydrochloric acid; compound (I) was then extracted with 25 ml of 5% sodium bicarbonate solution. Treatment with active carbon at room temperature and careful acidification with concentrated hydrochloric acid led to isolation of 1.3 g of yellow prisms. The product was purified by conversion to the sodium salt and recrystallized from a small quantity of chloroform; m. p. 115° (decomp.). The compound dissolves in methyl and ethyl alcohol, acetone, chloroform and ethyl acetate; it is poorly soluble in water.

Found %: C 41.97, 41.88; H 4.71, 4.59; S 14.97. $C_7H_{11}O_4NS$. Calculated %: C 41.39; H 4.46; S 15.75.

The compound gives off carbon dioxide on melting.

5,6-Dihydro-6,6-dimethyl-5-carbomethoxy-$\Delta^{3,4}$-thiazin-3-carboxylic acid (II). To 3 g of the hydro-

chloride of the methyl ester of DL-penicillamine [2] were added 2.55 g of bromopyruvic acid and 30 ml of chloroform; 6.6 ml of triethylamine was then added gradually with stirring and cooling to 0°. The reaction mass gradually turned orange-yellow. Compound (II) was isolated as described above. It was purified by reprecipitation from the sodium salt. Light-yellow prisms. Yield 2.4 g (70%); m. p. 132-133° (decomp.). Soluble in the same solvents.

Found %: C 46.76; H 6.03; N 6.15; S 14.43; CH_3O 13.18. $C_9H_{13}O_4NS$. Calculated %: C 46.75; H 5.67; N 6.05; S 13.79; CH_3O 13.37.

Methyl bromopyruvate. The literature method [3] involves rapid addition of bromine to methyl pyruvate. This can lead to sudden liberation of hydrobromic acid and ejection of the reaction mass. In our procedure the methyl pyruvate was first treated with dry hydrogen chloride.

After dry hydrogen chloride had been passed through 20 g of methyl pyruvate for one minute, 32 g of bromine was gradually added from a dropping funnel. Bromination proceeded quietly and quickly. At the conclusion of the reaction, the light-yellow oil was heated in vacuo (15-20 mm) at 30-50° with the objective of eliminating hydrogen bromide; it was finally distilled at 6-7 mm and 84-87°. Yield 25.9 g (73%).

5,6-Dihydro-3-carbomethoxy-$\Delta^{3,4}$-thiazin-5-carboxylic acid. 0.8 g of cysteine hydrochloride, 1 g of methyl bromopyruvate and 3 ml of anhydrous dioxane were left at room temperature in a sealed tube for 3 days. The precipitate was filtered and recrystallized twice from a mixture of methanol and acetone. The white crystals of cystine hydrochloride melted at 187-188° (decomp.).

Found %: C 23.64; H 4.38. $C_6H_{14}O_4N_2S_2Cl_2$. Calculated %: C 23.00; H 4.50.

The mother liquor was diluted with 25 ml of water and extracted several times with ether. The compound was extracted from the ether solution with 5% sodium bicarbonate solution, and after acidification with sulfuric acid it was again extracted with ether. The ethereal solution was dried with magnesium sulfate and the ether was distilled off to leave a volume of 10 ml; cooling of the latter for several days led to separation of yellow crystals with m. p. 143-145°(decomp.).

Found %: C 41.26, 41.49; H 4.20, 4.49; N 6.63; CH_3O 14.75. $C_7H_9O_4NS$. Calculated %: C 41.44; H 4.46; N 6.89; CH_3O 15.27.

SUMMARY

A number of derivatives of 5,6-dihydro-$\Delta^{3,4}$-thiazin-3,5-dicarboxylic acids were prepared.

LITERATURE CITED

[1] D. B. Sprinson and E. Chargaff, J. Biol. Chem. 164, 417 (1946).

[2] The Chemistry of Penicillin. USA, Princeton (1949).

[3] R. Kuhn and K. Dury, Lieb. Ann. 571, 44 (1951).

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INVESTIGATIONS ON CONJUGATED SYSTEMS

LXXXII. INFRARED SPECTRA OF VINYLACETYLENIC AND DIENIC ETHERS

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In previous communications we characterized the infrared spectra of some vinylacetylenic hydrocarbons and alcohols (the $C \equiv C-C=C$ conjugated system), as well as of acetylenic aldehydes and ketones (the $C \equiv C-C=O$ conjugated system) [1-3]. Continuing the study of the relation between structure, physical properties and reactivity, we have investigated the infrared spectra of some vinylacetylenic and dienic ethers with the general formulas: $R-C \equiv C-COR=CH_2$ and $R-CH=CH-COR=CH_2$.

The spectra of very few enolic ethers have hitherto been prepared [4]. We found no data in the literature for the spectra of ethers with conjugated multiple bonds.

Results of our measurements allow us to draw the following conclusions.

In the region of about 3300 cm^{-1} only an ether with a terminal acetylenic grouping absorbs intensively. The same phenomenon was also observed in the spectra of vinylacetylenic hydrocarbons and alcohols [1, 2]. In the spectra of acetylenic ketones, absorption of medium intensity was observed in this region also for compounds containing an acetylenic grouping in the middle of the chain [3].

In the region of valence CH vibrations (3150-2800 cm^{-1}) all of the ethers have 5 to 6 similar frequencies (in the various homologs). At least three of these belong to valence CH vibrations in alkyl radicals, possibly with superposition of other frequencies (for vinylacetylenic ethers: 2979, 2907-2924 and 2833 cm^{-1}; for dienic ethers: 2994, 2924 and 2809 cm^{-1}).* The 2870-2880 cm^{-1} appears in the spectra of compounds containing ethyl or larger radicals. Higher frequencies (3140 and 3020-3040 cm^{-1}) are associated with the presence of the CH_2 group. A frequency higher than 3100 cm^{-1} appears in the spectra of many compounds containing this group; it usually has a low intensity, however.

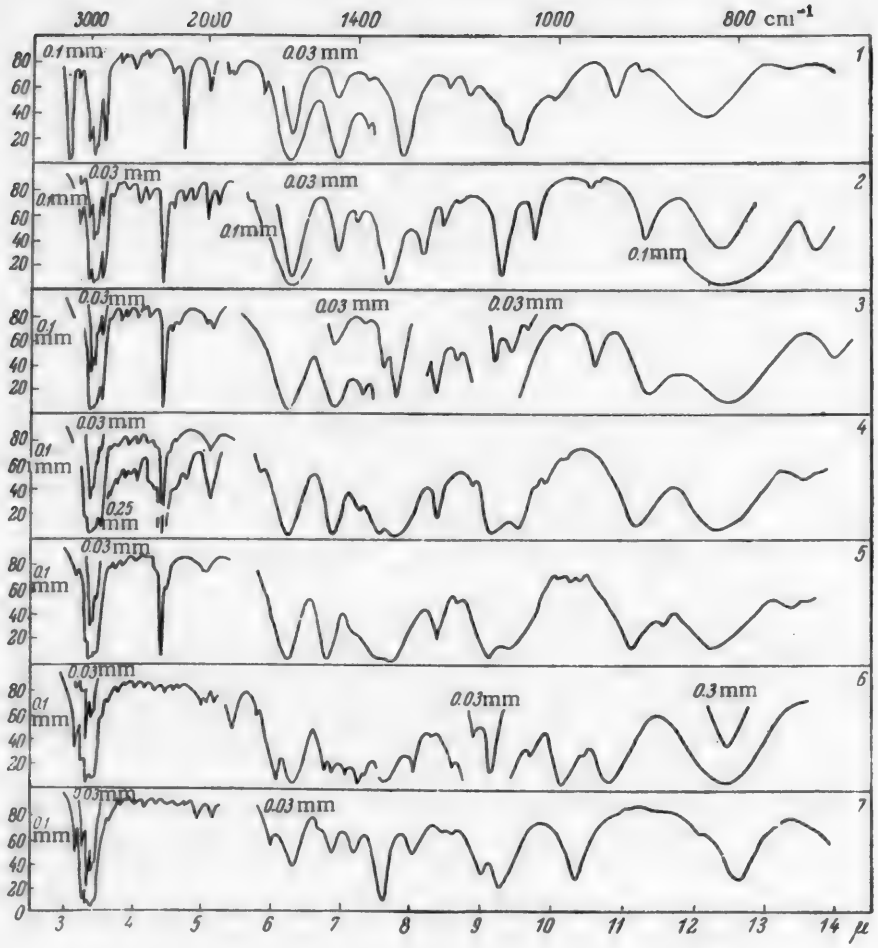
In the region of planar deformation CH vibrations, the spectra of vinylacetylenic ethers have not been closely characterized. There are usually 3-4 bands with values of frequencies differing little between the homologs. The band at 1450 cm^{-1} probably consists of 2 or 3 undifferentiated bands. In the spectra of dienic ethers these bands are resolved and a previously noted regularity is observed: the $CH_2=$ and $-CH_2-$ groups are associated respectively with absorption at 1414 and 1475 cm^{-1} [1].

Nonplanar deformation CH vibrations in the $CH_2=C$ grouping are represented in the spectra of vinylacetylenic ethers by an extremely characteristic band at 890 cm^{-1}. A dienic ether with a vinyl group absorbs at 923 and 985 cm^{-1}. The $-CH=CH-$ grouping corresponds to absorption at 960 cm^{-1}. These regularities are observed in the spectra of the most diverse unsaturated compounds [6, 7].

The triple bond of 3-methoxybuten-3-yne corresponds to a frequency of 2137 cm^{-1} in the spectrum, i.e., higher than in vinylacetylenic hydrocarbons and analogous structure (2114 cm^{-1}) [1]. In the spectra of other ethers with the structure of disubstituted acetylenes, the triple bond likewise corresponds to a higher frequency than in the spectra of hydrocarbons. The intensity of the frequency in question is higher than in the spectra of hydrocarbons and lower than in the spectra of acetylenic aldehydes and ketones.

Absorption bands corresponding to the double bond do not appreciably differ in the spectra of vinylacetylenic ethers from the same bands in the spectra of hydrocarbons in respect of position and intensity.

*The same frequencies appeared in the spectra of dimethyl ether and CH_3OH [5].



Infrared transmission spectra: 1) 2-methoxybuten-1-yne-3; 2) 2-methoxypenten-1-yne-3; 3) 2-methoxyhexen-yne-3; 4) 2-methoxyhepten-1-yne-3; 5) 2-methoxyocten-1-yne-3; 6) 2-ethoxybutadiene-1,3; 7) 2-ethoxypentadiene-1,3.

A similar picture is observed in the spectra of dienic ethers. The frequency of the symmetrical vibrations of the dienic system here has the usual value for hydrocarbons, but the frequency of the unsymmetrical vibrations is considerably lowered. In the spectra of similarly constituted dienic halogenated derivatives a marked lowering of both frequencies in comparison with the values in hydrocarbons is observed [9]. Consequently, a halogen atom more strongly deforms the dienic system than an alkoxy group.

This observation may be correlated with the susceptibility to polymerization of dienic ethers and halogenated derivatives. It is well-known that 2-ethoxybutadiene polymerizes 2000 times slower than chloroprene and only 3 times faster than isoprene [8].

The ether groups of dienic and vinylacetylenic ethers differ in reactivities; dienic ethers very much more easily undergo hydrolysis. In this connection it is of interest to compare the ν_{O-C} frequencies in the spectra of these two series of compounds. This is not yet possible, however, due to difficulties in plotting of the frequencies in the region where bands resulting from vibrations of the ether group can be expected. In the spectra that we investigated, these vibrations are presumably associated with bands in the 1150-1200 cm^{-1} region and possibly also in the region of approximately 1000 cm^{-1}.

$HC\equiv C-C(OCH_3)=CH_2$	$CH_3-C\equiv C-C(OCH_3)=CH_2$	$C_2H_5-C\equiv C-C(OCH_3)=CH_2$	$C_3H_7-C\equiv C-C(OCH_3)=CH_2$	$C_4H_9-C\equiv C-C(OCH_3)=CH_2$	$CH_2=CH-C(OC_2H_5)=CH_2$	$CH_3-CH=CH-C(OC_2H_5)=CH_2$
3300 (s)	—	—	—	—	—	—
3145 (w)	3140 (m)	3140 (m)	3140 (m)	3140 (w)	3140 (s)	3140 (m)
3025 (s)	3021 (s)	—	3021*(s)	3021*(s)	3044*(s)	3040 (s)
2979 (s)	2979 (s)	2979 (s)	2979 (s)	2979 (s)	2994 (s)	2994 (s)
2907*(s)	2915*(s)	2933 (s)	2941*(s)	2950*(s)	2924 (s)	2924 (s)
—	—	2874*(s)	2874 (s)	2874 (s)	2882*(s)	2882*(s)
2833 (s)	2833 (s)	2833 (s)	2833 (s)	—	2809 (m)	—
2725 (vw)	2725 (w)	2725 (w)	2725 (w)	2725 (w)	2747 (s)	2725*(s)
2646 (w)	2660 (vw)	2618 (w)	2660 (w)	2660 (w)	2618 (vw)	2604 (vw)
2591 (vw)	2577 (w)	2577 (vw)	2584 (w)	2584 (w)	2558 (vw)	—
2513 (w)	—	—	2532 (vw)	—	—	—
2475 (vw)	2475 (w)	2475 (w)	2481 (w)	2481 (vw)	2469 (vw)	2463 (vw)
2415 (w)	—	2415 (vw)	—	—	—	—
2392*(w)	2387 (w)	2387 (w)	2387*(w)	2387 (w)	2392 (vw)	2387 (vw)
—	—	—	2315*(w)	—	2299 (vw)	2299 (vw)
—	**2268** (s)	**2268** (s)	**2262** (s)	**2262** (s)	—	—
2218 (w)	2218 (w)	2188 (w)	—	—	2232 (vw)	—
2137 (s)	2134 (w)	2151 (w)	2110 (w)	2151 (vw)	2155 (vw)	—
2—	2066 (w)	2058 (vw)	—	—	2096 (vw)	2083 (vw)
1984 (m)	1984 (m)	1984 (w)	1961 (w)	1976 (w)	2000 (w)	2012 (w)
—	1961 (w)	1953 (w)	—	—	1969 (w)	—
—	1930 (w)	1930 (w)	—	—	1923 (w)	1923 (w)
1855 (vw)	—	—	—	—	—	—
1821 (vw)	—	—	—	—	1835 (m)	1835 (vw)
1718 (vw)	—	—	—	—	1721*(m)	—
1603 (s)	**1603** (s)	**1603** (s)	**1603** (s)	**1608** (s)	**1645** (s)	**1664** (s)
—	—	—	—	—	**1575** (s)	**1575** (s)
—	—	—	—	—	1475 (s)	1475*(m)
1453 (s)	1453 (s)	1453 (s)	1456 (s)	1456 (s)	1449 (s)	1449 (s)
—	—	—	—	—	1414 (s)	—
1368 (s)	1392 (s)	1374 (s)	1377*(s)	1377*(s)	1374 (s)	1381 (s)
—	—	1328 (s)	1330*(s)	1330*(s)	1357*(s)	—
—	—	—	—	—	1309 (s)	1309 (s)
1277 (s)	1292 (s)	1289 (s)	1292 (s)	1292 (s)	1241 (s)	1244 (s)
1195 (s)	1192 (s)	1196 (s)	1196 (s)	1193 (s)	1202 (m)	1180 (m)
1155 (m)	1156 (m)	1153 (m)	1153 (m)	1153 (m)	1159*(s)	1156 (m)
—	—	—	—	—	1120 (s)	1107 (s)
1078*(s)	1086 (s)	1092 (s)	1096 (s)	1096 (s)	1092*(s)	1075 (s)
—	—	—	—	1060 (s)	—	—
1058 (s)	1031 (s)	1040 (s)	1049 (s)	1040*(s)	1029*(s)	—
—	—	—	1026*(m)	—	—	—
1005*(s)	—	—	1005*(s)	994 (w)	—	—
—	978 (w)	988 (w)	979*(w)	975 (w)	985 (s)	963 (s)
—	956 (m)	943 (m)	—	963 (w)	954*(s)	—
916 (s)	—	—	—	—	923 (s)	911*(m)
894*(m)	889 (s)	882 (s)	895 (s)	895 (s)	—	—
—	—	—	—	864 (m)	—	—
826 (s)	811 (s)	824 (s)	817 (s)	818 (s)	800*(s)	826*(s)
737 (m)	733 (m)	—	741 (m)	741 (m)	758*(m)	790 (s)
701 (m)	—	718 (m)	—	728 (m)	—	—

• Frequencies marked with a star are superposed on other frequencies. Frequencies of a conjugated system of multiple bonds are in bold type.

•• (s) – strong, (w) – weak, (vw) – very weak, (m) – medium.

EXPERIMENTAL

The work was carried out with the substances previously described [10-12]. More accurate constants were obtained for some of the ethers. We give them in the following order: b. p. (at 20 mm), d_4^{20}, n_D^{20}.

$CH_3-C\equiv C-C(OCH_3)=CH_2$: 39°, 0.8832, 1.4690.
$C_2H_5-C\equiv C-C(OCH_3)=CH_2$: 52.5 — 53°, 0.8724, 1.4675.
$C_3H_7-C\equiv C-C(OCH_3)=CH_2$: 67 — 67,5°, 0.8686, 1.4662.
$C_4H_9-C\equiv C-C(OCH_3)=CH_2$: 84—84.5°, 0.8657, 1.4660.

Infrared spectra were photographed with the IKS-2 apparatus. Working conditions are given in the preceding papers. The experimental data are presented in the Diagram and in the Table.

SUMMARY

1. Infrared spectra of a series of vinylacetylenic and 1,3-dienic ethers were investigated (2-methoxybuten-1-yne-3; 2-methoxypenten-1-yne-3; 2-methoxyhexen-1-yne-3; 2-methoxyhepten-1-yne-3; 2-methoxyocten-1-yne-3; 2-ethoxybutadiene-1,3; and 2-ethoxypentadiene-1,3).

2. Some regularities in the position and intensity of absorption bands corresponding to systems of multiple bonds were noted.

LITERATURE CITED

[1] A. A. Petrov, Iu. I. Porfir'eva and G. I. Semenov, J. Gen. Chem. 27, 1167 (1957).*

[2] A. A. Petrov and G. I. Semenov, J. Gen. Chem. 27, 2941 (1957).*

[3] A. A. Petrov and G. I. Semenov, J. Gen. Chem. 27, 2947 (1957).*

[4] Kirrmann and Chencel, Bull. Soc. Chim. 1954, 1338.

[5] H. Herzberg, Vibrational and Rotational Spectra [Russian translation] (Foreign Lit. Press, 1949).

[6] L. G. Bellamy, The Infrared Spectra of Complex Molecules, London (1954).

[7] W. H. T. Davison and G. P. Bates, J. Chem. Soc. 1953, 2607.

[8] A. A. Petrov, Prog. Chem. 21, 452 (1952).

[9] A. A. Petrov, G. I. Semenov and N. P. Sopov, J. Gen. Chem. 27, 928 (1957).*

[10] A. A. Petrov, J. Gen. Chem. 10, 1682 (1940).

[11] A. A. Petrov and Iu. I. Porfir'eva, Proc. Acad. Sci. USSR, 90, 561 (1953).

[12] T. A. Zyrianova and A. A. Petrov, J. Gen. Chem. 26, 1918 (1956).*

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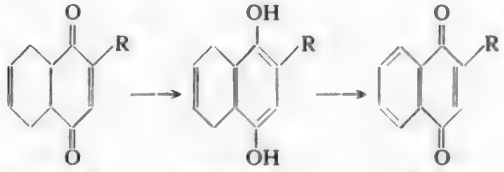
INVESTIGATIONS ON QUINONES

XX. PREPARATION OF NAPHTHOQUINONES AND DIHYDROANTHRAQUINONES

A. N. Grinev and A. P. Terent'ev

Methods of synthesis of p-naphthoquinones based on oxidation of 1-amino-4-hydroxynaphthalenes [1, 2], 1,4-diaminonaphthalenes [3], naphthalene [4], 2-methylnaphthalene [5], etc. [6, 7] either lead to low yields of 1,4-naphthoquinones [3-7] or are inconvenient in practice [1, 2]. Condensation of p-benzoquinone and toluquinone with butadiene has also been utilized for the preparation of 1,4-naphthoquinone (VII) and 2-methyl-1,4-naphthoquinone (VIII).



(I) R=H
(II) R=CH_3
(III) R=Cl

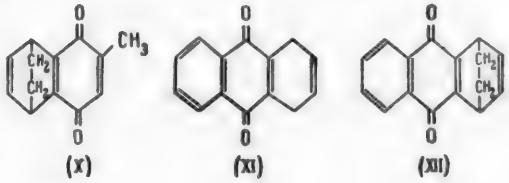
(IV) R=H
(V) R=CH_3
(VI) R=Cl

(VII) R=H
(VIII) R=CH_3
(IX) R=Cl

Although adducts of p-quinones with butadiene (I), (II) and (III) are obtained in yields close to the quantitative, complications arise through isomerization of the adducts to the substituted hydroquinones (IV), (V) and (VI). For example, the isomerization by hydrobromic acid of larger quantities of adducts than 5-10 g leads according to our observations to secondary reactions. We found that isomerization goes especially well on short-period heating of the adducts with acetic acid at the boil. We effected oxidation of hydroquinones (IV), (V) and (VI) to quinones (VII), (VIII) and (IX) with chromic acid. The preparation of adducts (I), (II) and (III), their isomerization and the oxidation of hydroquinones (IV), (V) and (VI) were realized without separation of intermediate compounds. 1,4-Naphthoquinone (VII) and 2-methyl-1,4-naphthoquinone (VIII) were obtained in 77-83% yield (calculated on the p-benzoquinone and toluquinone).

We previously synthesized p-quinones of the dihydronaphthalene series with the help of potassium bromate in an acid medium; this was found to be a very convenient oxidant [10]. The relatively poorly accessible dihydronaphthoquinones were obtained by this method in nearly quantitative yield.

In the present work we oxidized hydroquinones with potassium bromate and obtained 5,8-endoethylene-5,8-dihydro-2-methyl-1,4-naphthoquinone (X), 1,4-dihydroanthraquinone (XI) and 1,4-endoethylene-1,4-dihydroanthraquinone (XII).



(X) (XI) (XII)

The reaction was conducted under conditions similar to those described in our preceding papers [10, 11].

EXPERIMENTAL*

1. 1,4-Naphthoquinone (VII). 600 ml of acetic acid in a thick-walled flask was saturated (ice-cooling) with 101 g of butadiene. To the resultant solution was added 145 g of p-benzoquinone. The reaction vessel was tightly closed and stood for 48 hours at room temperature. The adduct (I) was isomerized by refluxing of the reaction solution for 4 hours at the boiling point of acetic acid. The resultant hydroquinone (IV) solidified to a dense, white crystalline mass. One liter of acetic acid was added to the reaction mixture to dissolve the hydroquinone. An aqueous solution of chromic acid (prepared by dissolving 307 g of chromic oxide in 307 ml of water) was gradually added to the solution with stirring by a mechanical stirrer. The chromic acid solution was added at such a speed that the temperature of the reaction mixture did not exceed 70-75°. The mixture was then heated for an hour at 70-75°. The solution was cooled to room temperature and diluted with sevenfold volume of water. The 1,4-naphthoquinone (VII) was filtered off and dried. M. p. 124°, in agreement with the literature [4]. Yield 167 g (77%).

2. 2-Methyl-1,4-naphthoquinone (VIII). Adduct (II) was prepared from 30 g of toluquinone, 30 g of butadiene and 150 ml of acetic acid. After isomerization as described above, 200 ml of acetic acid was added to the reaction mixture. The hydroquinone (V) was oxidized with aqueous chromic acid prepared from 54 g of chromic oxide and 54 ml of water. All of the operations were performed as in Experiment 1. M. p. of 2-methyl-1,4-naphthoquinone (VIII) 104-105°. The literature [9] reports m. p. 104°. Yield 36.6 g (83.6%).

3. 2-Chloro-1,4-naphthoquinone (IX). Adduct (III) was prepared from 75 g of chloro-p-benzoquinone, 42 g of butadiene and 300 ml of acetic acid. After isomerization, the reaction solution was diluted with 500 ml of acetic acid. Hydroquinone (VI) was oxidized with chromic acid prepared from 119 g of chromic oxide and 119 ml of water. The operations were performed as in Experiment 1. M. p. of 2-chloro-1,4-naphthoquinone 117°, in agreement with the literature [12]. Yield 40 g (38.6%).

4. 2-Methyl-5,8-endoethylene-5,8-dihydronaphthohydroquinone. The adduct of toluquinone with cyclohexadiene with m. p. 88° (3.2 g), prepared by the known method [13], was dissolved in acetic acid and boiled for 4 hours (gentle boiling of the acetic acid). The resultant solution was diluted with water. An oily layer separated out and crystallized on cooling. 3 g of crystals of the hydroquinone was obtained. M. p. 175-176°; literature: m. p. 177° [13].

5. 2-Methyl-5,8-endoethylene-5,8-dihydro-1,4-naphthoquinone (X). To a solution of 3 g of 2-methyl-5,8-endoethylene-5,8-dihydroanthraquinone in 30 ml of dioxane was added a hot solution of 1.5 g of potassium bromate and 1.5 ml of 1 N sulfuric acid in 15 ml of water. The reaction mixture was heated for 2-3 minutes to form a transparent, yellow solution; this was cooled and diluted with 100 ml of water. Crystals of quinone (X) were collected and dried in a vacuum-desiccator over calcium chloride. M. p. 84-85°. Literature: m. p. 85-86° [13]. Yield 2.8 g.

6. 1,4-Dihydroanthrahydroquinone. The adduct of 1,4-naphthoquinone with butadiene with m. p. 104-105°, prepared by the literature method [14], was isomerized by heating with acetic acid as above. 1,4-Dihydroanthrahydroquinone came out of the acetic acid solution in the form of white crystals which very quickly darken in the air. Yield 3.5 g (from 4 g of adduct). M. p. 205-207° (from aqueous alcohol).

Found %: C 79.45, 79.32; H 5.34, 5.43. $C_{14}H_{12}O_2$. Calculated %: C 79.22; H 5.70.

7. 1,4-Dihydroanthraquinone (XI). The experiment was performed with 3 g of 1,4-dihydroanthrahydroquinone, 1.5 g of potassium bromate, 30 ml of dioxane, 15 ml of water, and 1.5 ml of 1 N sulfuric acid. The procedure was the same as for Experiment 5. 2.6 g of the quinone (XI) was obtained with m. p. 210°. Literature: m. p. 208-210° [15].

8. 1,4-Dihydro-1,4-endoethyleneanthrahydroquinone. The adduct from 1,4-naphthoquinone and cyclohexadiene (m. p. 135°), obtained by the published procedure [15], was isomerized by heating with acetic acid as described above. 4.5 g of adduct gave 4 g of 1,4-dihydro-1,4-endoethyleneanthrahydroquinone. M. p. 200-202° (from aqueous alcohol).

*Carried out with participation of V. K. Lomova.

Found %: C 80.93, 80.95; H 5.90, 5.63. $C_{16}H_{14}O_2$. Calculated %: C 80.64; H 5.92.

9. 1,4-Dihydro-1,4-endoethyleneanthraquinone (XII). The experiment was carried out with 3 g of 1,4-dihydro-1,4-endoethyleneanthrahydroquinone, 1.5 g of potassium bromate, 30 ml of dioxane, 15 ml of water and 1.5 ml of sulfuric acid. Procedure as above. Yield of the quinone (XII) 2.7 g. M. p. 176-178°. Literature: m. p. 180° [15].

SUMMARY

1. It was shown that isomerization of adducts of quinones with dienic hydrocarbons by heating in acetic-acid solutions leads smoothly to substituted hydroquinones.

2. A method was developed for the preparation of 1,4-naphthoquinone, 2-methyl-1,4-naphthoquinone and 2-chloro-1,4-naphthoquinone; it involved reaction of p-benzoquinone, toluquinone and chloro-p-benzoquinone with butadiene without isolation of intermediate compounds.

3. Oxidation of the corresponding hydroquinones with potassium bromate in an acid medium by the previously developed procedure gave 2-methyl-5,8-dihydro-5,8-endoethylene-1,4-naphthoquinone, 1,4-dihydroanthraquinone and 1,4-dihydro-1,4-endoethyleneanthraquinone.

LITERATURE CITED

[1] J. Conant and L. Fieser, J. Am. Chem. Soc. 46, 1862 (1924).

[2] R. Harman and J. Cason, J. Org. Ch. 17, 1058 (1952).

[3] C. Liebermann, Lieb. Ann. 183, 242 (1876).

[4] O. Miller, J. Russ. Chem. Soc. 16, 414 (1884).

[5] N. S. Nikolaev, J. Gen. Chem. 15, 654 (1945).

[6] R. Arnold and R. Larson, J. Org. Ch. 5, 250 (1940).

[7] P. Monnet, F. Reverdin and E. Nolting, Ber. 12, 2306 (1879).

[8] L. Fieser, J. Am. Chem. Soc. 70, 3165 (1948).

[9] G. I. Ostrozhinskaia, J. Gen. Chem. 16, 1053 (1946).

[10] A. N. Grinev, A. B. Terent'ev and A. P. Terent'ev, J. Gen. Chem. 26, 560 (1956).*

[11] A. N. Grinev and A. P. Terent'ev, J. Gen. Chem. 25, 2145 (1955).*

[12] Th. Zincke and O. Kegel, Ber. 21, 1039 (1888).

[13] M. Grdinic and V. Jugovic, Arh. Kem. 23, 73 (1951).

[14] O. Diels and K. Alder, Lieb. Ann. 460, 98 (1928).

[15] O. Diels and K. Alder, Ber. 62, 2337 (1929).

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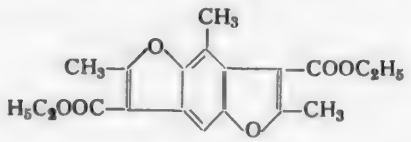
INVESTIGATIONS ON QUINONES

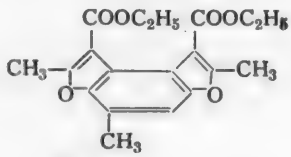
XXI. THE STRUCTURE OF SUBSTANCES PREPARED BY CONDENSATION OF TOLUQUINONE AND α-NAPHTHOQUINONE WITH ETHYL ACETOACETATE

A. N. Grinev and A. P. Terent'ev

Graebe and Levy [1], who investigated the reaction of toluquinone with ethyl acetoacetate, found that this reaction gives a mixture of two compounds with m. p. 173 and 122°. Due to the death of one of the authors, however, no further work was carried out in this field [1]. In one of our investigations we recently established that the compound with m. p. 120-122° is formed predominantly if the reaction is performed with rapid addition of toluquinone to a mixture of ethyl acetoacetate, zinc chloride and alcohol while heating [2]. Two possible structures can be advanced for this compound (I) and (II):

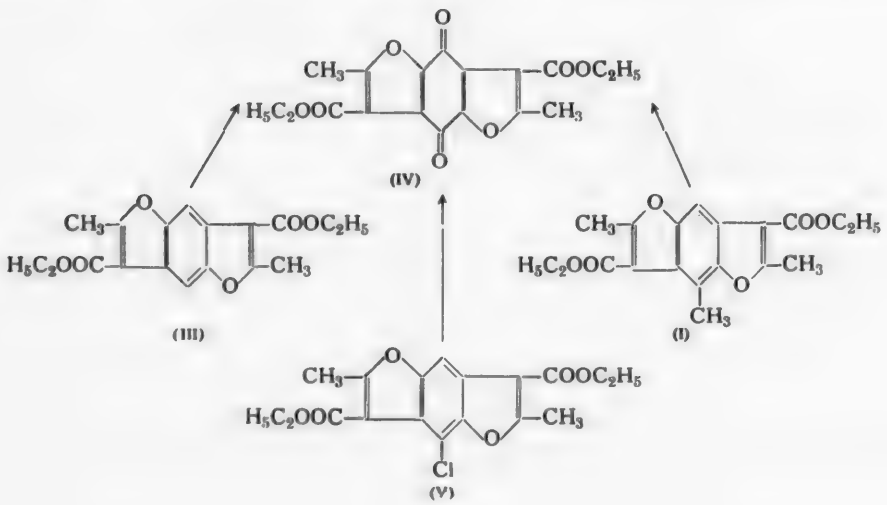


(I)



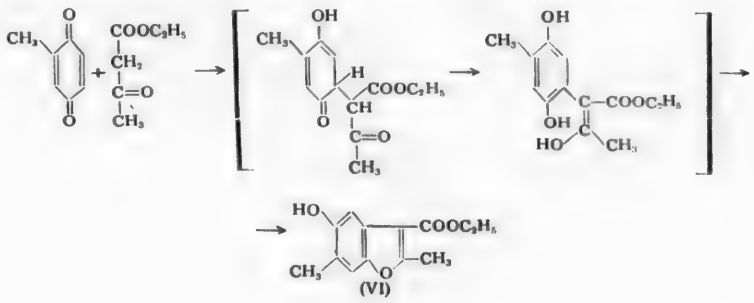
(II)

By oxidation with chromic acid of the diethyl ester of 2,6-dimethylbenzo-(1,2-b; 4,5-b')-difuran-3,7-dicarboxylic acid (III) we obtained the quinone (IV) of the benzodifuran series. According to our observations, quinone (IV) is obtained, in poor yield it is true, by oxidation of chlorine-substituted benzodifuran (V). Since the same compound is also formed by oxidation of the benzodifuran derivative resulting from condensation of toluquinone with ethyl acetoacetate, we can assume that this substance is the diethyl ester of 2,4,6-trimethylbenzo-(1, 2-b; 4,5-b')-difuran-3,7-dicarboxylic acid (I).



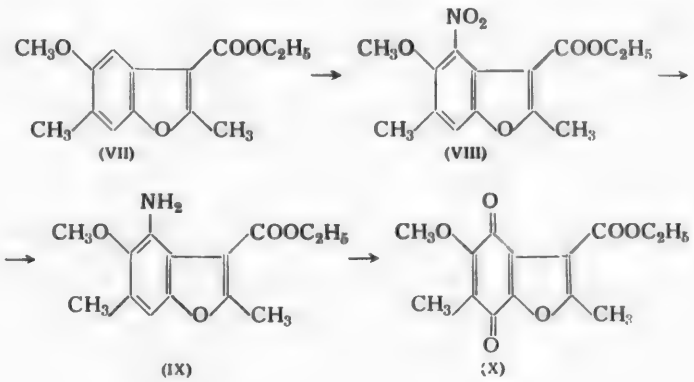
The structural formulas of compounds (III) and (V) are not in doubt [3-5].

The ethyl ester of 2,6-dimethyl-5-hydroxybenzofuran-3-carboxylic acid (VI) with m. p. 173° is obtained in 43% yield by condensation of toluquinone with ethyl acetoacetate in an alcoholic solution of zinc chloride when the toluquinone is added very slowly.



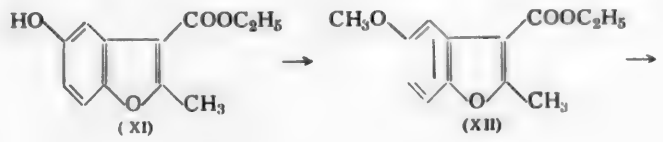
(VI)

Consequently, in this case the CH_3 group in the p-quinone nucleus directs the molecule of ethyl acetoacetate into the position opposite to the substituent, or (by analogy with the benzene series) into the para-position. The structure of the substituted benzofuran (VI) was confirmed by the following route:

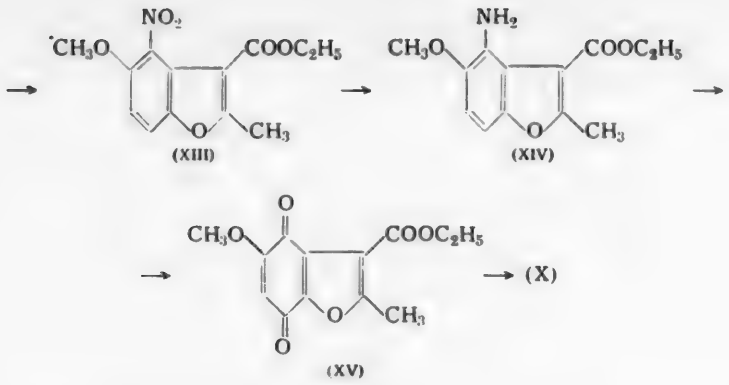


(VII) (VIII) (IX) (X)

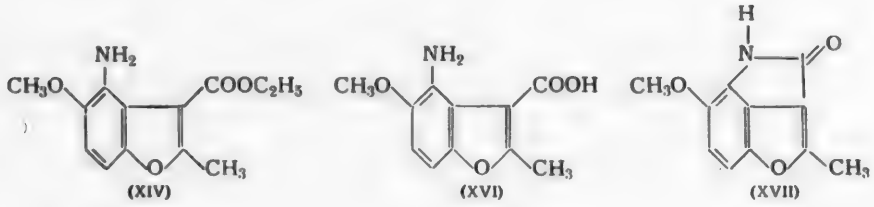
The ethyl ester of 2,6-dimethyl-5-methoxybenzofuran-3-carboxylic acid (VII) was prepared by methylation of (VI) with dimethyl sulfate. Nitration of (VII) with nitric acid (d 1.43) in acetic acid leads to the ethyl ester of 2,6-dimethyl-4-nitro-5-methoxybenzofuran-3-carboxylic acid (VIII); reduction of the latter over platinum catalyst gives the corresponding amino compound (IX). Compound (IX) is oxidized by potassium dichromate in a sulfuric acid medium to the ethyl ester of 2,6-dimethyl-5-methoxybenzofuranquinone-3-carboxylic acid (X), but in insignificant yield. We prepared the quinone (X) from the known [6] ethyl ester of 2-methyl-5-hydroxybenzofuran-3-carboxylic acid (XI) by a similar series of transformations.



(XI) (XII)

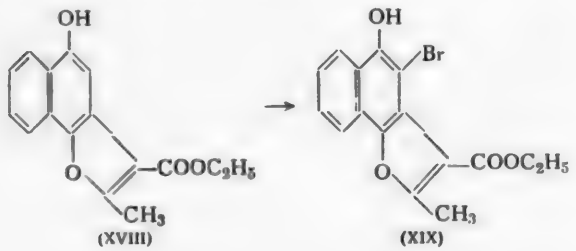


The ethyl ester of 2-methyl-5-methoxybenzofuranquinone-3-carboxylic acid was methylated with lead tetraacetate by Fieser's procedure [7]. The structure of the ethyl ester of 2-methyl-4-amino-5-methoxybenzofuran-3-carboxylic acid (XIV) was confirmed by cyclization (by heating) of the aminoacid (XVI), obtained by hydrolysis of the ester (XIV), to the amide (XVII).

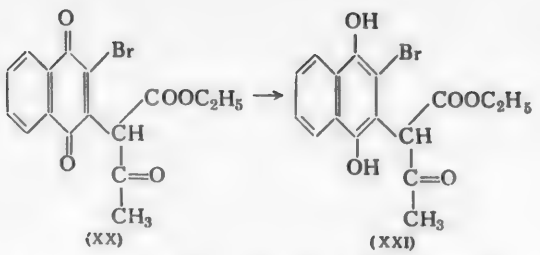


Condensation of p-benzoquinone with ethyl acetoacetate and ethyl benzoylacetate, as our investigations have shown [6, 8], proceeds with initial formation of carbon-carbon bonds, since the reaction leads to 5-hydroxy-substituted benzofurans.

On the basis of these observations, we can assume that also the reaction of α-naphthoquinone with ethyl acetoacetate, previously studied by us [9], leads to the ethyl ester of 2-methyl-5-hydroxy-α-naphthofuran-3-carboxylic acid (XVIII). With the objective of obtaining more definite proof of the structure of the α-naphthofuran (XVIII), we attempted to synthesize by reverse synthesis the ethyl ester of 2-methyl-4-bromo-5-hydroxy-α-naphthofuran-3-carboxylic acid (XIX) prepared from it.

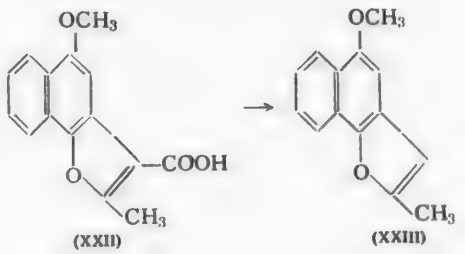


As the starting substance for the reverse synthesis we chose the 3-acetoacetic ester of 2-bromo-1,4-naphthoquinone (XX) prepared by Liebermann [10]. Reduction of the latter with zinc in acetic acid gave the corresponding hydroquinone (XXI).



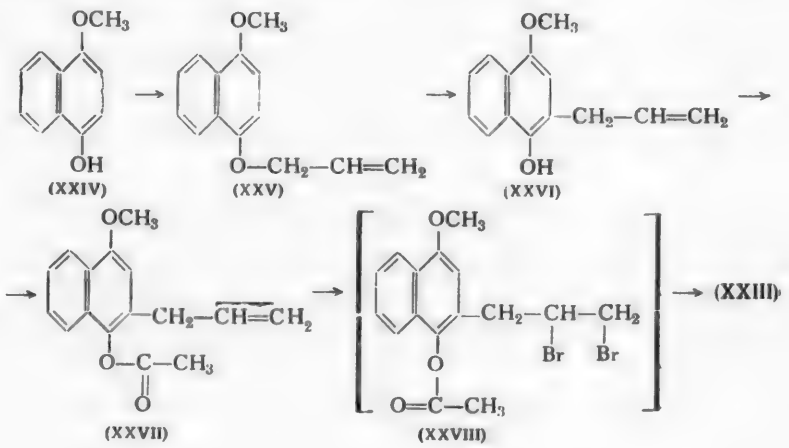
(XX) (XXI)

Complications ensued, however, during the cyclization of the hydroquinone (XXI) to the naphthofuran (XIX) under the action of both zinc chloride and sulfuric acid. We then carried out the proof of the structure of the naphthofuran (XVIII) by the method once applied by us [6], namely: the 2-methyl-5-methoxy-α-naphthofuran-3-carboxylic acid (XXII) [9] prepared from the naphthofuran (XVIII) was converted by decarboxylation into 2-methyl-5-methoxy-α-naphthofuran (XXIII).



(XXII) (XXIII)

The naphthofuran (XXIII) was synthesized from the known [11] 4-methoxy-1-hydroxynaphthalene (XXIV) by the Claisen reaction [12] according to the scheme:



(XXIV) (XXV) (XXVI) (XXVII) (XXVIII) (XXIII)

EXPERIMENTAL

1. Diethyl ester of 2,6-dimethylbenzo-(1,2,-b;4,5-b')-difuroquinone-3,7-dicarboxylic acid (IV). a) To a solution of 10.2 g of benzodifuran (III) in 197 ml of acetic acid was added a solution of chromic acid

(prepared from 24.7 g of chromic oxide, 16 ml of water and 132 ml of 98% acetic acid) in the course of an hour with stirring and gentle boiling of the acetic acid. The reaction solution was diluted with double the volume of water. The crystals of the quinone (IV) were filtered, dried and twice recrystallized from acetic acid. Yield 6.5 g. The quinone (IV) has good solubility in acetic acid, dioxane and dichloroethane; m. p. 103-104° (from acetic acid).

Found %: C 59.93, 59.86; H 4.68, 4.72. $C_{18}H_{16}O_8$. Calculated %: C 60.00; H 4.48.

b) An experiment was performed with 3 g of benzodifuran (V), 70 ml of acetic acid, and a solution of chromic acid prepared from 8 g of chromic oxide, 4 ml of water, and 45 ml of 98% acetic acid. The reaction and isolation of the product were carried out as in experiment (a). The yield after recrystallization from acetic acid was 0.9 g; m. p. of (IV) 103-104° (from acetic acid). A mixed melting test with the quinone (IV) prepared in experiment (a) did not give a depression of melting point.

c) An experiment was run with 2.5 g of benzodifuran (I) and 60 ml of 98% acetic acid. The chromic acid solution was prepared from 7 g of chromic oxide, 4 ml of water and 35 ml of acetic acid (98%). Reaction and isolation of product were carried out as before. Yield of quinone (IV) 0.6 g; m. p. 103-104° (from acetic acid). A mixed melting test with the quinone (IV) obtained in experiment (a) did not give a depression of melting point.

2. Ethyl ester of 2,6-dimethyl-5-hydroxybenzofuran-3-carboxylic acid (VI). The experiment was performed in accordance with our procedure in a Soxhlet without a siphon [13]. 28 grams of zinc chloride was dissolved in 30 ml of anhydrous alcohol in the flask of the Soxhlet with heating. To the resultant solution were added 52 g of ethyl acetoacetate and 20 ml of absolute ether. 24 grams of toluquinone was placed in the thimble of the Soxhlet. The flask was heated on an air bath at 90-100° (thermometer in bath), and the Soxhlet discharged 15-17 drops per minute. The toluquinone was extracted from the thimble into the reaction flask for 15 hours, after which heating was carried out for 45 minutes at 95-100°. The crystals that deposited after cooling of the reaction liquid were collected and recrystallized from methanol and dichloroethane-acetone mixture (1 : 1). Yield of benzofuran (VI) 20 g, m. p. 173° (in agreement with the literature [1]).

Found %: C 67.02, 67.04; H 6.30, 6.18. $C_{13}H_{14}O_4$. Calculated %: C 66.65; H 6.02.

3. Ethyl ester of 2,6-dimethyl-5-methoxybenzofuran-3-carboxylic acid (VII). 11.7 g of the hydroxybenzofuran (VI) was dissolved in 40 ml of dioxane. The solution was mixed with 50 ml of 2 N sodium hydroxide. To the suspension of phenate was added 12.6 g of dimethyl sulfate and the mixture was shaken for 35 minutes at room temperature. The transparent reaction solution was diluted with two volumes of water and cooled. The crystals of methoxybenzofuran (VII) were collected and recrystallized from alcohol. Yield 13 g, m. p. 123-124° (from alcohol).

Found %: C 67.80, 67.94; H 6.74, 6.78. $C_{14}H_{16}O_4$. Calculated %: C 67.73; H 6.50.

4. Ethyl ester of 2,6-dimethyl-4-nitro-5-methoxybenzofuran-3-carboxylic acid (VIII). 1.7 ml of nitric acid (d 1.43) was added in 15 minutes (with ice-cooling and stirring) to a solution of 3.4 g of benzofuran (VII) in 30 ml of glacial acetic acid; the mixture was then left at room temperature; the temperature rose to 25°. The mixture was heated at 37-40° for 1 hour. 2.5 volumes of water were added and the mass was cooled. A viscous layer separated; this was rubbed with a glass rod in presence of a little alcohol and gave crystals of the nitro compound (VIII). Yield after recrystallization from alcohol 2.9 g, m. p. 112-113°.

Found %: C 57.49, 57.60; H 5.32, 5.40. $C_{14}H_{15}O_6N$. Calculated %: C 57.33; H 5.16.

5. Ethyl ester of 2,6-dimethyl-4-amino-5-methoxybenzofuran-3-carboxylic acid (IX). 1.5 g of nitro compound (VIII) was mixed with 30 ml of anhydrous alcohol in a glass hydrogenating vessel; 0.1 g of platinum oxide was added. The mixture was shaken in a hydrogen atmosphere for 7 hours. The catalyst and unreacted nitro compound were filtered off and washed on the filter with a little ether. The filtrates were evaporated in vacuo in the absence of air and the precipitate was dissolved in a little absolute ether. Gradual evaporation of the ether was accompanied by separation of crystals of amine (IX). Yield 0.6 g after recrystallization from a mixture of ligroine with alcohol; m. p. 106°.

Found %: C 63.76, 63.64; H 6.56, 6.60. $C_{14}H_{17}O_4N$. Calculated %: C 63.86; H 6.51.

6. Ethyl ester of 2,6-dimethyl-5-methoxybenzofuroquinone-3-carboxylic acid (X). To a suspension of 1 g of amine (IX) in 35 ml of water were added (with cooling) 5 ml of conc. sulfuric acid and 0.6 g of pulverized potassium dichromate. The reaction mixture was left overnight at room temperature. An additional 0.6 g of potassium dichromate was then added and the mixture was left for 3 hours. The quinone was extracted from the precipitate and the aqueous layer with ether; the ethereal extracts were combined and dried with calcium chloride. Evaporation of the ether left 0.12 g of quinone (X) with m. p. 116-117° (from alcohol).

Found %: C 60.56, 60.64; H 4.77, 4.86. $C_{14}H_{14}O_6$. Calculated %: C 60.43; H 5.07.

7. Ethyl ester of 2-methyl-5- methoxybenzofuran-3-carboxylic acid (XII). Methylation of the hydroxybenzofuran (XI) was performed as above (experiment 3). Reaction components were 44 g of hydroxybenzofuran (XI), 200 ml of 2 N sodium hydroxide, 40 ml of dimethyl sulfate and 80 ml of dioxane. Yield of methoxybenzofuran (XII) 50 g; m. p. 46-47° (from alcohol).

Found %: C 66.63, 66.60; H 5.99, 5.90. $C_{13}H_{14}O_4$. Calculated %: C 66.65; H 6.02.

8. Ethyl ester of 2-methyl-4-nitro-5-methoxybenzofuran-3-carboxylic acid (XIII). The experiment was performed with 21 g of methoxybenzofuran (XII), 11.1 ml of nitric acid (d 1.43), 150 ml of acetic acid. The nitric acid was added at 20° in the course of 30 minutes. The mass was held at 35-37° for 1 hour. The reaction liquid was diluted with three volumes of water and cooled; the precipitate was collected and recrystallized twice from a mixture of alcohol and dioxane (4:1). Yield of nitro compound (XIII) 17 g; m. p. 146-148°.

Found %: C 56.18, 56.14; H 4.60, 4.70. $C_{13}H_{13}O_6N$. Calculated %: C 55.91; H 4.70.

9. Ethyl ester of 2-methyl-4-amino-5-methoxybenzofuran-3-carboxylic acid (XIV). Reduction of nitro compound (XIII) was effected as described above (experiment 5). The experiment was carried out with 8.4 g of nitro compound (XIII), 0.1 g of platinum oxide and 50 ml of anhydrous alcohol. The reaction period was 4 hours. Catalyst and unreacted nitro compound (XIII) were separated and the filtrate was worked up as before. 1.8 g of crystals of amine (XIV) was obtained by recrystallization from a mixture of ligroine and alcohol; m. p. 127-128°.

Found %: C 62.47, 62.44; H 6.29, 6.22. $C_{13}H_{15}O_4N$. Calculated %: C 62.64; H 6.07.

Treatment of amine (XIV) with hydrochloric acid in the usual manner gave the hydrochloride with m. p. above 180° (with decomp.).

Found %: C 54.53, 54.47; H 5.54, 5.60. $C_{13}H_{16}O_4NCl$. Calculated %: C 54.66; H 5.64.

10. Ethyl ester of 2-methyl-5-methoxybenzofuroquinone-3-carboxylic acid (XV). Oxidation of amine (XIV) to the quinone (XV) was effected as described above (experiment 6). Components were 3 g of amine (XIV), 3.6 g of potassium diochromatex and 15 ml of conc. sulfuric acid. Yield of quinone (XV) 0.35 g; m. p. 155-157° (from aqueous dioxane).

Found %: C 59.00, 58.88; H 4.60, 4.63. $C_{13}H_{12}O_6$. Calculated %: C 59.09; H 4.58.

11. Ethyl ester of 2,6-dimethyl-5-methoxybenzofuroquinone-3-carboxylic acid (X). Methylation of quinone (XV) with lead tetraacetate was effected by the known procedure [7]. 0.5 g of quinone (XV) was dissolved in 10 ml of glacial acetic acid, and 0.3 g of malonic acid and 2.5 g of lead tetraacetate were added. The reaction mixture was heated at 50-60° for an hour on a air bath. 2.5 g of lead tetraacetate was added and heating continued for 1.5 hours at 75°. The reaction mixture was poured into water, the precipitated quinone (X) was collected and recrystallized from alcohol. Yield of purified quinone 0.15 g; m. p. 116°. A mixed melting test with quinone (X) obtained in experiment 6 did not give a depression of melting point.

12. 2-Methyl-4-amino-5-methoxybenzofuran-3-carboxylic acid (XVI). 0.1 g of sodium hydroxide was dissolved in 6 ml of alcohol, and 6 ml of ether and 0.5 g of amine (XIV) were added. The reaction mixture was refluxed in a small flask, shielded against contact with air by a Bunsen valve, for 1 hour at 60-80°. The reaction liquid was diluted with 3 volumes of water and acidified with dilute hydrochloric acid (litmus test). In the vicinity of the neutral point, the light-green acid (XVI) came down. Yield 0.38 g; m. p. >220° (decomp.) after recrystallization from a mixture of ethyl alcohol and ligroine (1 : 5).

Found %: C 59.65, 59.68; H 4.88, 4.92. $C_{11}H_{11}O_4N$. Calculated %: C 59.72; H 5.01.

13. Inner amide of 2-methyl-4-amino-5-methoxybenzofuran-3-carboxylic acid (XVII). 0.2 g of amino acid (XVI) was heated for 1 hour with 2 ml of quinoline at 180-220°; the cooled reaction solution was treated with dilute hydrochloric acid; the crystals of amide (XVII) were collected and recrystallized from nitrobenzene. Yield 0.1 g; m. p. 193-195°.

Found %: C 64.90, 64.85; H 4.60, 4.49. $C_{11}H_9O_3N$. Calculated %: C 65.02; H 4.46.

14. Ethyl ester of 2-methyl-4-bromo-5-hydroxy-2-naphthofuran-3-carboxylic acid (XIX). To a solution in 30 ml of dioxane of 3 g of the naphthofuran (XVIII), prepared by us previously [9], was added dioxane dibromide prepared by dissolving 0.17 g of bromine in 5 ml of dioxane. The resultant transparent, light-yellow solution was diluted with water and cooled. The crystals of bromoderivative (XIX) were collected and recrystallized from alcohol. Yield 3.6 g; m. p. 93-94°.

Found %: Br 22.75, 22.80. $C_{16}H_{13}O_4Br$. Calculated %: Br 22.92.

15. Bromonaphthohydroquinone-acetoacetic ester (XXI). 5 g of bromo-α-naphthoquinone-acetoacetic ester (XX) [10] was dissolved in acetic acid in the cold. To the solution was added zinc powder in small portions with gentle heating until the the solution had decolorized. The solution was separated from the deposit and diluted with water. The crystals were collected and recrystallized from alcohol. Yield of the hydroquinone (XXI) 3 g; m. p. 114-116°.

Found %: C 51.99, 52.15; H 4.09, 4.12. $C_{16}H_{15}O_5Br$. Calculated %: C 52.31; H 4.09.

16. 2-Methyl-5-methoxy-α-naphthofuran (XXIII). A mixture of 9.6 g of the methoxy acid (XXII) [9] and 5.6 g of calcium oxide was heated in a Wurtz flask over a bare flame; a syrupy oil distilled over; the latter was taken up in ether, dried with calcium chloride and distilled at reduced pressure. Yield of naphthofuran (XXIII) 4 g; b. p. 154-155° (1 mm).

Found %: C 79.29, 79.36; H 5.85, 5.88. $C_{14}H_{12}O_2$. Calculated %: C 79.22; H 5.70.

The picrate of the naphthofuran, prepared in the usual manner, melted at 131-132° (from alcohol).

Found %: C 54.58, 54.49; H 3.44, 3.42. $C_{20}H_{15}O_9N_3$. Calculated %: C 54.43; H 3.43.

17. Allyl ether of 4-methoxy-1-naphthol (XXV). 28.6 g of 4-methoxy-1-naphthol (XXIV) [11], 35.5 ml of anhydrous acetone, 16.9 g of allyl bromide and 27.18 g of potassium carbonate were placed in a round-bottomed flask. The reaction mixture was heated on a water bath for 19 hours, then treated with water and extracted with ether. The ethereal extract was washed with 2 N sodium hydroxide and dried with calcium chloride. The viscous liquid product was distilled at reduced pressure. Yield of the allyl ether (XXV) 21 g, b. p. 140° (1 mm).

Found %: C 78.66, 78.73; H 6.76, 6.85. $C_{14}H_{14}O_2$. Calculated %: C 78.48; H 6.59.

18. 2-Allyl-4-methoxy-1-naphthol (XXVI). 14 grams of the allyl ether of 4-methoxy-1-naphthol (XXV) was heated at 240° on an oil bath in a vacuum of 22 mm for 1.5 hours; the 2-allyl-4-methoxy-1-naphthol (XXVI) was then distilled at reduced pressure. Yield 10.5 g; b. p. 155-156° (1 mm); m. p. 50° (from alcohol).

Found %: C 78.88, 78.96; H 6.71, 6.75. $C_{14}H_{14}O_2$. Calculated %: C 78.48; H 6.59.

19. 1-Acetoxy-2-allyl-4-methoxynaphthalene (XXVII). 7.68 g of 2-allyl-4-methoxy-1-naphthol (XXVI) was mixed with 8 ml of acetic anhydride, and a few drops of conc. sulfuric acid were added. The reaction mixture was heated for 1.5 hours on a water bath, cooled, and dissolved in ether. The ethereal solution was washed with dilute sodium hydroxide and dried with sodium sulfate. Compound (XXVII) was distilled at reduced pressure. Yield 6.5 g; b. p. 164-167° (1 mm); m. p. 91-92° (from alcohol).

Found %: C 75.19, 75.09; H 6.38, 6.33. $C_{16}H_{16}O_3$. Calculated %: C 74.98; H 6.29.

20. 2-Methyl-5-methoxy-α-naphthofuran (XXIII). 5.88 g of 1-acetoxy-2-allyl-5-methoxynaphthalene (XXVII) was dissolved in 6 ml of chloroform. To the cooled and stirred solution was added 1 ml of bromine in 8 ml of chloroform (dropwise). After bromination had been completed (evident from the decolorization of the solution), the chloroform was taken off in vacuo. The residual dibromo compound (XXVIII) was mixed with a saturated solution of 6 g of potassium hydroxide in methyl alcohol and heated for 31 hours on a water bath. The solution was separated from the potassium bromide, the alcohol was distilled off, and the resultant oil was taken up in ether and dried with calcium chloride. Yield of naphthofuran (XXIII) 1.4 g; b. p. 154-155° (1 mm). The picrate melted at 131°. A mixed melting test with 2-methyl-5-methoxy-α-naphthofuran (XXIII) from experiment 16 did not give a depression of melting point.

SUMMARY

1. The structure of the products of condensation of toluquinone and α-naphthoquinone with ethyl acetoacetate was confirmed.

2. When the reaction of toluquinone with ethyl acetoacetate is carried out slowly, the methyl group of toluquinone directs the molecule of ethyl acetoacetate into the para-position.

3. A number of substituted benzofurans, benzodifurans and naphthofurans were prepared.

LITERATURE CITED

[1] G. Graebe and S. Levy, Lieb. Ann. 283, 245 (1894).

[2] A. P. Terent'ev, A. N. Grinev and Pan Bon Khvar, J. Gen. Chem. 24, 2050 (1954).*

[3] M. Ykuta, J. pr. Ch. (2), 45, 66 (1892).

[4] E. Bernatek and F. Thoresen, Acta Chem. Scand. 5, 743 (1955).

[5] A. N. Grinev, Pan Bon Khvar, V. N. Frosin and A. P. Terent'ev, J. Gen. Chem. 26, 561 (1956).*

[6] A. N. Grinev, Pan Bon Khvar and A. P. Terent'ev, J. Gen. Chem. 26, 2928 (1956).*

[7] L. Fieser, J. Am. Chem. Soc. 64, 2048 (1942).

[8] A. N. Grinev, Pan Bon Khvar and A. P. Terent'ev, J. Gen. Chem. 27, 821 (1957).*

[9] A. N. Grinev, V. N. Frosin and A. P. Terent'ev, J. Gen. Chem. 25, 523 (1955).*

[10] C. Liebermann, Ber. 32, 263 (1899).

[11] U. S. Patent, 2272822 (1951); Ch. A. 1953, 32876.

[12] L. Claisen, Lieb. Ann. 418, 69 (1910).

[13] A. N. Grinev, Pan Bon Khvar and A. P. Terent'ev, J. Gen. Chem. 27, 1087 (1957).*

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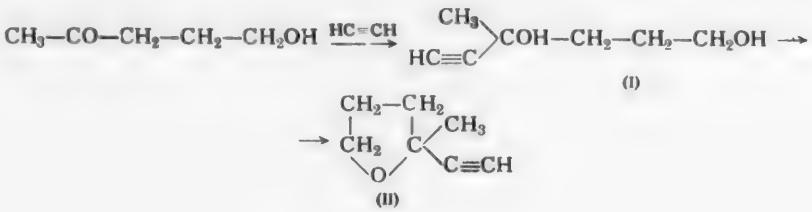
THE MECHANISM OF THE DEHYDRATION OF γ-GLYCOLS

V. STUDY OF THE PROPERTIES AND TRANSFORMATIONS OF THE ACETYLENIC γ-GLYCOL 3-METHYL-1-HEXYN-3,6-DIOL

T. A. Favorskaia and O. V. Sergievskaia

In preceding communications [1, 2] we showed that the alcohols 2-phenyl-2-penten-5-ol and 3-methyl-3-hexen-1-yne-6-ol, which contain a system of conjugated double bonds, do not isomerize to the corresponding tetrahydrofuran derivatives under the mild conditions that we employed for a series of β-ethylenic alcohols [3, 4]. Transformation of 2-phenyl-2-penten-5-ol into 2,2-methylphenyltetrahydrofuran required very much more drastic conditions, while the enynic alcohol completely resinified under these conditions.

Wishing to prepare 2,2-methylethynyltetrahydrofuran (II), which we required for further syntheses, we synthesized the acetylenic γ-glycol 3-methyl-1-hexyn-2,6-diol (I), in the expectation that, like other investigated γ-glycols [3, 4] it would be dehydrated to the tetrahydrofuran derivative on treatment with very dilute sulfuric acid.



(I)

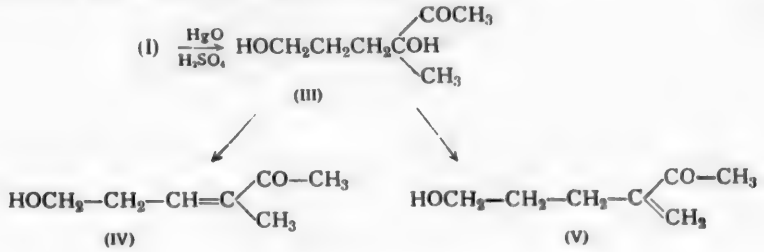
(II)

Condensation of acetopropyl alcohol with acetylene was effected by the method of A. E. Favorskii. The resultant glycol was an extremely unusual compound. Its most striking feature was that it did not react under ordinary conditions with ammoniacal silver oxide; a precipitate of silver derivative was formed only on heating of the reaction mixture nearly to the boil; the precipitate of silver derivative is poorly soluble in nitric acid; it formed a yellowish powder; it detonated when an attempt was made to weigh it for analysis.

On the other hand, on heating the glycol with potassium hydroxide solution, it broke down to acetopropyl alcohol and acetylene; the quantity of hydrogen taken up on hydrogenation over platinum black corresponded to the presence of a triple bond in the glycol molecule. Ozonization of the glycol yielded about 40% of formic acid; oxidation with potassium permanganate was unsuccessful, but oxidation with nitric acid (5 volumes of acid to 1 volume of water) gave acetone and acetic and levulinic acids. The glycol was hydrated in presence of Kucherov catalyst to the anticipated ketoglycol (III) in 69% yield. This was a crystalline substance which on standing with 2,4-dinitrophenylhydrazine solution gave a precipitate of the 2,4-dinitrophenylhydrazone; complete analysis of this compound revealed, however, that its composition corresponds not to a derivative of the ketoglycol but to a derivative of the unsaturated ketoalcohol; evidently on standing with a sulfuric acid solution of 2,4-dinitrophenylhydrazine the ketoglycol undergoes dehydration, and the resultant ketoalcohol reacts with the 2,4-dinitrophenylhydrazine. The ketoglycol itself does not form a 2,4-dinitrophenylhydrazone.

Hydration of the glycol gave a small quantity of low-boiling fraction which distilled over a fairly wide range; it yielded 2,4-dinitrophenylhydrazone whose composition corresponded to the derivative of the unsaturated ketoalcohol but which melted at a temperature different from that of the 2,4-dinitrophenylhydrazone described above. Consequently, treatment of the glycol with a sulfuric acid solution of mercuric oxide leads to partial dehydration of the ketoglycol with formation of some other unsaturated ketoalcohol.

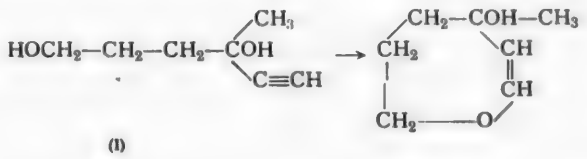
Dehydration of the ketoglycol can proceed in two directions:



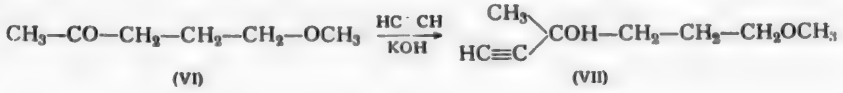
In order to establish which of the two ketoalcohols is formed when the ketoglycol is stood with a sulfuric acid solution of 2,4-dinitrophenylhydrazine, we stood the ketoglycol with a sulfuric acid solution of the same concentration but obtained no ketoalcohol at all; the ketoglycol was recovered unchanged; this signifies that 2,4-dinitrophenylhydrazine has some catalytic action, and in its absence the ketoglycol does not undergo dehydration.

The presence of a carbonyl group in the molecule of the ketoglycol was confirmed by plotting of the ultraviolet absorption spectrum.

Consequently, all of the properties and transformations of the glycol, as well as the spectrographic data (infrared and Raman), compel us to assign the formula (I) to it; and explanation was still lacking, however, for the inability of the glycol to react with ammoniacal silver oxide at room temperature. It might be suggested that the glycol possesses another structure and acquires structure (I) under the influence of reactants or high temperature. It is well-known [3, 4] that the hydrogen of the primary alcoholic group in β-ethylenic alcohols easily migrates to the β-carbon atom to form tetrahydrofuran derivatives. We suspected that the hydrogen of the primary alcohol group of glycol (I) migrates to the δ-carbon atom with formation of an unstable seven-membered oxide ring which is readily cleaved under the influence of reagents.



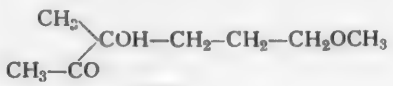
We therefore decided to replace the primary hydroxyl of the glycol by a methoxy group and to thereby obtained a compound with a free acetylenic hydrogen. For this purpose it was necessary to prepare the methyl ether of acetopropyl alcohol and to condense it with acetylene. We were able to prepare this ether only by reacting acetopropyl alcohol with dimethyl sulfate, all of the other common methods of synthesis of ethers being unsuccessful in the present case. The prepared ether (VI) was condensed with acetylene in presence of pulverized potassium hydroxide.



The behavior of ether (VII) towards ammoniacal silver oxide was entirely similar to that of glycol (I): the silver derivative only came down when the reaction mixture was heated. Consequently, the hypothesis of the transformation of the glycol into a cyclic compound by migration of the hydroxyl hydrogen to the δ-carbon atom proved to be untenable, and it was necessary to seek for another explanation of this unusual behavior of the glycol and its ether towards ammoniacal silver oxide solution. With this objective we made a close study of the properties of ether (VII).

The presence of a triple bond in the molecule of the ether was confirmed through the Raman spectrum, as well as by hydrogenation and ozonolysis; the latter reaction gave about 65% of formic acid.

The ether was hydrated by the Kucherov procedure; the resultant carbonyl



(VIII)

compound (VIII) corresponded in composition to the above formula, and the ultraviolet spectrum confirmed the presence of the carbonyl group; nevertheless, compound (VIII) did not react either with 2,4-dinitrophenylhydrazine or with semicarbazide. We may recollect that the ketoglycol (III), as such, also did not react with 2,4-dinitrophenylhydrazine, only the product of its dehydration (the unsaturated ketoalcohol) entering into reaction. On the other hand, it is well-known [2] that the product of dehydration of glycol (III) – the enynic alcohol 3-methyl-3-hexen-1-yn-6-ol – differs from the glycol in instantaneously reacting in the cold with ammoniacal silver oxide solution. The impression is created that in order for the acetylenic hydrogen and the carbonyl group in the compounds in question to manifest their inherent properties the neighboring tertiary hydroxyl group must be absent. However, all of the known acetylenic alcohols with the general formula $RR'COH-C\equiv CH$ immediately give precipitates with the silver reagent [5-7], and the products of their hydration react with semicarbazide and 2,4-dinitrophenylhydrazine [8]. Whatever role is also played by the terminal hydroxyl and methoxyl groups present in one of the radicals, in their absence the reactions with the reagents in question proceed normally. The data obtained are certainly as yet insufficient for a conclusive explanation of the anomalous behavior of the glycol and its derivatives, and further investigations of this problem are necessary.

EXPERIMENTAL

Synthesis of 3-methyl-1-hexyn-3,6-diol (I). The γ-glycol was prepared by condensation of acetopropyl alcohol with acetylene in presence of pulverized potassium hydroxide under the conditions worked out for the synthesis of acetylenic glycols by A. E. Favorskii and A. S. Onitsenko [9]. The yield of glycol was 30-40% reckoned on the acetopropyl alcohol entering into reaction. In spite of many fractional distillations, the glycol always contained a trace of acetopropyl alcohol which gives a precipitate of 2,4-dinitrophenylhydrazone with m. p. 143°. The glycol only ceased to react with 2,4-dinitrophenylhydrazine after treatment with a freshly prepared solution of sodium bisulfite; its ultraviolet spectrum then demonstrated the absence of a carbonyl group.

B. p. 136.5° (17 mm), n_D^{20} 1.4718, d_4^{20} 1.0220, MR_D 35.06. $C_7H_{10}O_2$ F. Calculated 35.57.

Found %: C 65.61; H 9.55; number of active H 1.94. M 145 (in dioxane). $C_7H_{10}O_2$. Calculated %: C 65.51; H 9.45; number of active H 2. M 128.

Hydrogenation of 3-methyl-1-hexyn-3,6-diol. 11.5 g of glycol was hydrogenated in anhydrous alcohol in presence of 1.2 g of platinum black. Ninety-two percent of the theoretical quantity of hydrogen was absorbed, calculated for the triple bond. The isolated product was fractionally distilled at 12 mm. The following fractions were obtained:

1st, 126-129°, 2 g, n_D^{20} 1.4540; 2nd, 129-130.5°, 8.5 g, n_D^{20} 1.4572, d_4^{20} 0.9607, MR_D 37.43; calcd. 37.57.

The constants found are in agreement with the literature data for 3-methylhexane-3,6-diol [10].

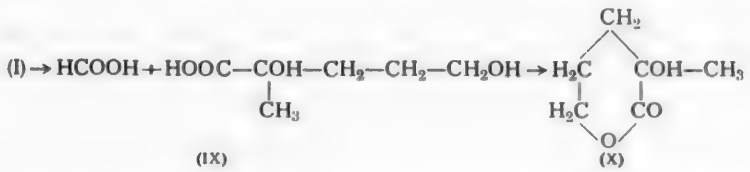
Decomposition of 3-methyl-1-hexyn-3,6-diol [I] with alkali. Heating of glycol (I) with 40% potassium hydroxide solution led to evolution of acetylene which gave a characteristic precipitate of silver derivative; the residue was acetopropyl alcohol (2,4-dinitrophenylhydrazone with m. p. 143°).

Oxidation of glycol (I) with nitric acid. 8 grams of the glycol was dissolved in a mixture of 50 ml of conc. nitric acid and 10 ml of water, and the solution was heated on a water bath for 1/2 hour until commencement of a violent reaction accompanied by liberation of CO_2 and oxides of nitrogen. After an hour, the reaction mixture was neutralized with potassium carbonate solution and the neutral products were distilled into a solution of 2,4-dinitrophenylhydrazine. The melting point of the 2,4-dinitrophenylhydrazone was 124°; no depression in admixture with acetone 2,4-dinitrophenylhydrazone. The solution of the salts was evaporated to dryness and extracted with alcohol for elimination of resinous impurities. After the alcohol had been driven off, the residue was acidified with sulfuric acid and the volatile acids were distilled off with steam. Heating with silver carbonate gave the silver salt of a volatile acid (acetic).

Found %: Ag 64.70. $C_2H_3O_2Ag$. Calculated %: Ag 64.67.

A viscous, syrupy acid was isolated from the aqueous solution of the nonvolatile acids in the extractor and gave a 2,4-dinitrophenylhydrazone with m. p. 196-199°; a mixed test with the 2,4-dinitrophenylhydrazone of authentic levulinic acid did not give a depression. Consequently, the main product of oxidation was levulinic acid; acetic acid and acetone were formed as a result of its further oxidation. The residue of acetylene was oxidized to carbon dioxide.

Ozonization of 3-methyl-1-hexyn-3,6-diol (I). 3.1 g of the glycol was taken for ozonolysis. 1.44 g of ozone was used (124% reckoned on the triple bond). The ozonide was decomposed with water. Formic acid was determined in a part of the solution by Fincke's method [11] (40%). Steam distillation did not yield any neutral products. After acidification of the solution and distillation of the formic acid, the residue was extracted with ether in an extractor. The product gave a precipitate with a solution of 2,4-dinitrophenylhydrazone. Ozonization of 3-methyl-1-hexyn-3,6-diol could have been expected to lead to the lactone of α-methyl-α,δ-dihydroxyvaleric acid (X).



It is known that this type of lactone can react with phenylhydrazine to form a phenylhydrazide of the acid. Thus, valerolactone [12] reacts with phenylhydrazine to form the phenylhydrazide of hydroxyvaleric acid which, however, could not be isolated in a sufficiently pure form even after many recrystallizations.

The 2,4-dinitrophenylhydrazine derivative that we prepared was recrystallized with great difficulty, and its nitrogen content was rather lower than corresponded to the anticipated phenylhydrazide (15.51 instead of 17.83%). We therefore did not obtain adequate evidence of the identity of the compound.

The Raman spectrum of the glycol was prepared. It was necessary to work at 60° for this purpose because at the ordinary temperature in the light of the mercury lamp the viscous mass of glycol was observed to contain in suspension of small quantity of very fine crystals whose presence interfered with the plotting of the spectrum. The glycol did not crystallize, however, even after standing for 6 months, and the quantity of crystals had evidently not altered after this period of time. The 2108 cm^{-1} frequency, corresponding to the triple bond, was observed in the spectrogram.

Hydration of 3-methyl-1-hexyn-3,6-diol (I). 1 g of mercuric oxide was treated with a still hot mixture of 3.3 ml of conc. sulfuric acid and 100 ml of water; dropwise addition of 23 g of the glycol, dissolved

in 25 ml of water, was made to the solution obtained; the mass was then heated for 1 hour at 80°, after which the volatile products were distilled off with steam. The distillate was salted out and extracted with ether to give about 1 g of substance with b. p. 127-133° and n_D^{20} 1.4380, which rapidly decolorized $KMnO_4$ solution and gave a 2,4-dinitrophenylhydrazine with m. p. 128-130°.

Found %: C 50.86; H 5.19; N 17.96. $C_{13}H_{16}O_5N_4$. Calculated %: C 50.65; H 5.19; N 18.18.

Results of analyses are in accord with data calculated for the 2,4-dinitrophenylhydrazone of the unsaturated compound that could be formed by dehydration of the ketoglycol by one of the schemes presented above.

The nonvolatile products were extracted with ether in an extractor for 7-8 days. Removal of the ether left 18 g (65%) of colorless crystals with m. p. 84-85°.

Found %: C 57.49; H 9.72; OH 22.90. M 165. $C_7H_{14}O_3$. Calculated %: C 57.53; H 9.59; OH 23.25. M 146.

The results obtained correspond to the formula of the ketoglycol. The ketoglycol gives a precipitate with m. p. 108-109° on treatment with 2,4-dinitrophenylhydrazine solution, not immediately but only after standing overnight.

Found %: C 50.82; H 5.16; N 18.09. $C_{13}H_{16}O_5N_4$. Calculated %: C 50.65; H 5.19; N 18.18. $C_{13}H_{18}O_6N_4$. Calculated %: C 44.44; H 8.66; N 17.17.

The composition of the hydrazone obtained thus corresponds not to a ketoglycol derivative but to a derivative of the unsaturated ketoalcohol. In the ketoglycol itself the carbonyl group was detected by plotting of the ultraviolet absorption spectrum in ethyl alcohol solution with the SF-4 spectrograph. Absorption maximum at 286 mμ, log ε 1.164 (x 1 cm, c 0.02).

Preparation of the ether of acetopropyl alcohol by reaction with dimethyl sulfate in alkali solution. Thirty-four g of acetopropyl alcohol was dissolved in 40 ml of 40% potassium hydroxide solution, and 46 g of freshly distilled dimethyl sulfate (b. p. 186-189°) was run in at such a rate that the temperature of the reaction mixture rose to 70-90°; thereupon it was heated on a water bath at 40-50° for 1-2 hours. The following day the precipitated salts were filtered off and the solution was extracted with ether; after drying followed by removal of the ether, the residue was distilled at 10 mm. The following fractions were obtained:

1st, b. p. 48-52°, 9 g, n_D^{20} 1.4134; 2nd, b. p. 52.5-53.5°, 6.5 g, n_D^{20} 1.4141.

The yield of crude product was approx. 40%. The compound was redistilled in a column at atmospheric pressure.

B. p. 152-155°, n_D^{20} 1.4147, d_4^{20} 0.9228; MR_D 31.46; calcd. 31.52.

Found %: C 61.72; H 10.34; OCH_3 27.10. M 104. $C_6H_{12}O_2$. Calculated %: C 62.07; H 10.34; OCH_3 26.72. M 116.

Acetopropyl alcohol methyl ether gave a 2,4-dinitrophenylhydrazone with m. p. 64° (from alcohol) and a semicarbazone with m. p. 124° (from alcohol).

Found (for the semicarbazone) %: C 48.58; H 8.61. $C_7H_{15}O_2N_3$. Calculated %: C 48.55; H 8.66.

The following other methods of synthesis of the methyl ether of acetopropyl alcohol were tried out.

1) Reaction of the bromide of acetopropyl alcohol with sodium ethoxide. This reaction gave about 70% of acetyltrimethylene.

2) Methylation of acetopropyl alcohol with methyl iodide in an alkaline medium. The original substances were recovered unchanged (part of the methyl iodide was hydrolyzed).

3) Methylation with methyl alcohol saturated with hydrogen chloride. A mixture of acetopropyl alcohol and its corresponding chloride were obtained.

The ultraviolet absorption spectrum of the methyl ether of acetopropyl alcohol in ethyl alcohol was plotted with the SF-4 spectrograph; thickness of absorbing layer x, 1 cm; c 0.02 m. Absorption maximum at 276 mμ and log ε 1.383.

Reaction of acetopropyl methyl ether with acetylene. The conditions of the A. E. Favorskii reaction were employed. Distillation of the product gave the following two fractions:

1st, b. p. 111-113° (38 mm), 17 g, n_D^{20} 1.4469; 2nd, b. p. 113.5° (37 mm), 35 g, n_D^{20} 1.4490.

Yield of crude product 85%. It was purified from traces of original methoxy derivative by treatment with saturated sodium bisulfite solution.

B. p. 102-102.5° (19 mm) 192-194° (760 mm), n_D^{20} 1.4494, d_4^{20} 0.9474, MR_D 40.29. $C_8H_{14}O_2$ ∃. Calculated 40.31.

Found %: C 66.93; H 9.84; OCH_3 21.88; OH 4.008. M 157. $C_8H_{14}O_2$. Calculated %: C 67.60; H 9.86; OCH_3 21.83; OH 11.97. M 142.

The Raman spectrum of the prepared methoxy derivative of 3-methyl-1-hexyn-3,6-diol was plotted with Zeiss spectrograph at 25°. The frequency of 2107 cm^{-1} obtained is that of the characteristic vibration of the triple bond in monosubstituted acetylenes.

Analysis for hydroxyl by the Terent'ev method was carried out many times with various specimens, but the results were identical. 3-Methyl-6-methoxy-1-hexyn-3-ol therefore behaves anomalously not only towards ammoniacal silver oxide solution but also towards methyl magnesium iodide solution.

Hydrogenation of 3-methyl-6-methoxy-1-hexyn-3-ol. 1 g of the compound, 0.1 g of platinum black and 40 ml of anhydrous alcohol were taken. After 2 hours 336 ml of hydrogen had been taken up (101% of the theoretical calculated for the triple bond).

Ozonolysis of 3-methyl-6-methoxy-1-hexyn-3-ol. The quantity of ozone consumed was 104% of the theoretical, calculated for the triple bond. The ozonide was decomposed with water and the formic acid was determined by Fincke's method [11]; the amount found was 69.9%. No other acid products could be identified. Neutral products were not detected.

Hydration of 3-methyl-6-methoxy-1-hexyn-3-ol by the Kucherov method. 2.4 g of mercuric oxide was dissolved in a still mixture of 14 ml of sulfuric acid and 100 ml of water. 11 g of 3-methyl-6-methoxy-1-hexyn-3-ol was added dropwise to the cooled solution, and the temperature of the reaction mixture rose to 60-70°. When all had been added, the mass was heated to the boil for 2.5 hours. The reaction products were extracted with ether in an extractor; after drying and removal of solvent, the product was distilled in a vacuum of 18 mm. The following fractions were obtained:

1st, 92-97°, 0.8 g, n_D^{20} 1.4350; 2nd, 107-109°, 6.7 g, n_D^{20} 1.4360. The residue was a resin.

The yield of the 2nd fraction was 50% of the theoretical; it did not form derivatives with semicarbazide or 2,4-dinitrophenylhydrazone even on standing for many days; it slowly decolorized $KMnO_4$ solution; with ammoniacal silver solution it did not give a precipitate either in the cold or on boiling (indication of absence of starting product).

Constants of 3-methyl-6-methoxyhexan-2-one-3-ol: b. p. 107-109° (18 mm), n_D^{20} 1.4360, d_4^{20} 0.9913, MR_D 42.20; calcd. 42.32.

Found %: C 59.73; H 10.02; OCH_3 19.43; OH 10.92. M 159.8. $C_8H_{16}O_3$. Calculated %: C 60.00; H 10.00; OCH_3 19.04; OH 10.62. M 160.

The ultraviolet absorption spectrum of the methyl ether of the ketoglycol was plotted with the SF-4 spectrograph (x 1 cm; c 0.02 M); absorption maximum at 284 mμ and log ε 1.561.

The infrared spectrum of 3-methyl-6-methoxyhexan-2-one-3-ol was also plotted; the carbonyl group corresponded to the characteristic frequency of 1715 cm^{-1} (IKS-11 spectrometer).

SUMMARY

1. The acetylenic γ -glycol, 3-methyl-1-hexyn-3,6-diol, and its primary monomethyl ether, 3-methyl-6-methoxy-1-hexyn-3-ol, were synthesized.

2. Is was shown that both of these compounds do not react under ordinary conditions with ammoniacal silver oxide solution; only on boiling do they form light-yellow precipitates of the silver derivatives; the latter are soluble with difficulty in nitric acid; in the dry state they explode when being weighed out.

3. The presence of a triple bond in both of the compounds was demonstrated by hydrogenation, ozonization and oxidation, as well as by the Raman spectra.

4. The hydration of 3-methyl-1-hexyn-3,6-diol and its ether was studied. The resultant carbonyl compounds did not react with semicarbazide or 2,4-dinitrophenylhydrazine; the presence of a carbonyl group in both cases was established by the ultraviolet absorption spectra.

5. A 2,4-dinitrophenylhydrazone came down when the ketoglycol obtained by hydration of 3-methyl-1-hexyn-3,6-diol was stood with a sulfuric acid solution of 2,4-dinitrophenylhydrazine; it corresponded in composition to a derivative of the unsaturated ketoalcohol formed by dehydration of the ketoglycol.

6. It was shown that in the absence of 2,4-dinitrophenylhydrazine, the ketoglycol does not undergo dehydration under the influence of sulfuric acid of the same strength.

7. Methyl acetopropyl ether was prepared for the first time.

LITERATURE CITED

[1] T. A. Favorskaia and O. V. Sergievskaia, J. Gen. Chem. 25, 1509 (1955).*

[2] T. A. Favorskaia and L. S. Bresler, J. Gen. Chem. 27, 1179 (1957).*

[3] T. A. Favorskaia, N. V. Shcherbinskaia and E. S. Golovacheva, J. Gen. Chem. 23, 1878 (1953).*

[4] T. A. Favorskaia and N. P. Ryzhova, J. Gen. Chem. 26, 423 (1956).*

[5] T. A. Favorskaia, J. Gen. Chem. 9, 389 (1939).

[6] T. A. Favorskaia and A. I. Zakharova, J. Gen. Chem. 10, 446 (1940).

[7] T. A. Favorskaia and I. A. Favorskaia, J. Gen. Chem. 10, 451 (1940).

[8] T. A. Favorskaia and O. A. Zakhar'evskaia, J. Gen. Chem. Supp. Vol. II, 887 (1953).*

[9] A. E. Favorskii and A. S. Onishchenko, J. Gen. Chem. 11, 1111 (1941).

[10] T. A. Favorskaia and N. V. Shcherbinskaia, J. Gen. Chem. 23, 1667 (1953).*

[11] H. Fincke, Biochem. Z. 51, 253 (1913).

[12] W. Wislicenus, Ber. 20, 401 (1887).

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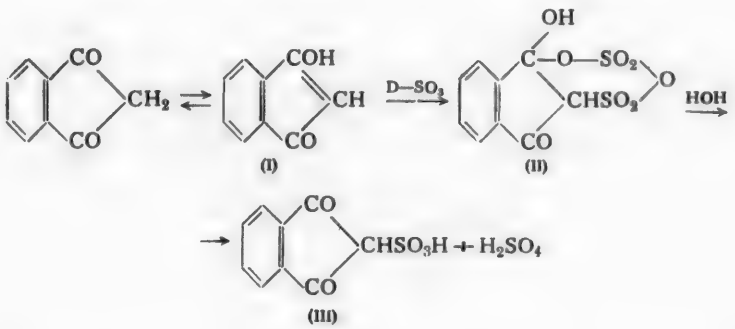
SULFONATION OF β-DIKETONES WITH DIOXANE SULFOTRIOXIDE

II. INDANDIONE-1,3-SULFONIC-2 ACID AND ITS SALTS

E. Iu. Gudrinietse, A. F. Ievin'sh and G. Ia. Vanag

It was shown in a previous communication [1] that indandione-1,3 was easily sulfonated by dioxane sulfotrioxide (D-SO_3) giving indandione-1,3-sulfonic-2 acid. The sulfonation was carried out in a solution of 1,2-dichloroethane at room temperature. It has been suggested in the literature [2] that the sulfonation may proceed by way of the enol form (I) giving an addition product (II) whose hydrolysis yields the corresponding sulfonic acid, in our case

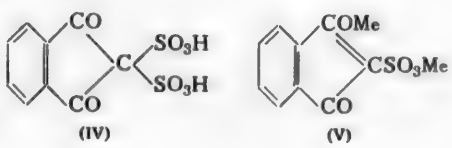


(I) (II) (III)

We did not, however, succeed in isolating the intermediate product (II). When indandione-1,3 is added to a solution of D-SO_3 in 1,2-dichloroethane, reaction takes place immediately, the solution becomes hot (water cooling!) and after 2-3 minutes indandione-1,3-sulfonic-2 acid (III) precipitates out. If the precipitate is dissolved in water, the solution does not give a reaction for the sulfate ion, which indicates that the intermediate product (II) was not formed.

It would appear that the reaction occurs directly with the hydrogen of the active methylene group in indandione-1,3; in other words indandione combines with the molecule of sulfuric anhydride to give indandione-1,3-sulfonic-2 acid (III).

If an excess of D-SO_3 is taken and the temperature is allowed to rise from 25 to 40° during the reaction, indandione-1,3-disulfonic-2,2 acid (IV) is formed; it is isolated as the sodium salt. It is interesting that the barium salt of this acid is very slightly soluble in water. Investigation of the disulfonic acid is proceeding and will form the subject of a separate report.



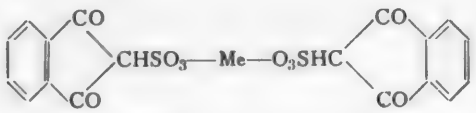
(IV) (V)

Indandione sulfonic acid (III) is a colorless crystalline substance which is hygroscopic in air. We did not succeed in recrystallizing the acid.

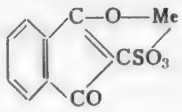
The sodium, potassium, lithium and ammonium salts were prepared by saturating the aqueous solution of indandione sulfonic acid with the appropriate chlorides. The indandione sulfonates obtained were yellowish or colorless crystalline substances, readily soluble in water, insoluble in alcohols and other organic solvents. The aqueous solutions of these salts are yellowish in color; when the solutions are acidified, the coloration disappears.

Treatment of the monosodium or monopotassium salt of indandione sulfonic acid gives the disodium (V, Me = Na) or dipotassium (V, Me = K) salts of this acid. They are precipitated by the addition of a small amount of ethanol. The dipotassium salt obtained corresponds in appearance and analytical findings to the same salt obtained by V. N. Ufimtsev [3]; however, no oxime could be obtained from it.

When an aqueous solution of indandione sulfonic acid is treated with strontium and barium ions, preferably at temperatures around zero, the corresponding salts (VI, Me = Sr, Ba) are obtained in crystalline form. The calcium salt could only be prepared in alcoholic solution; it is yellow and crystallizes with 2 molecules of water.



(VI)



(VII)

Salts obtained by neutralization of the aqueous solution of indandione sulfonic acid with carbonates of magnesium, calcium, strontium and barium are yellow crystalline substances containing 1 atom of metal per molecules of the acid. The salts obtained evidently have the structure (VII) (Me=Mg, Ca, Sr, Ba). The least water-soluble salt is the barium salt (0.10%), the strontium salt is rather more soluble (0.37%), and still more so the calcium salt (0.85%). The magnesium salt dissolves in water very readily.

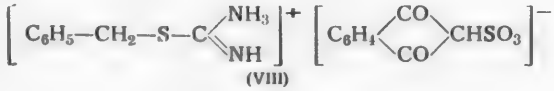
Neutralization of indandione sulfonic acid with carbonates of zinc, cadmium, manganese, nickel and cobalt gives salts of these substances which appear to have the structure (VII) (Me = Zn, Cd, Mn, Ni, Co). The zinc and cadmium salts are orange-yellow in color and crystallize with 2 molecules of water. The water of crystallization is removed at 150° and the salts become yellow.

The nickel, cobalt and manganese salts of type (VII) are of interest. They form complexes with pyridine. These may be promising with respect to preparation of complexes of a new type. Similar complexes of carboxylic acids are known in the literature [4]. How general this phenomenon might be will be revealed by further investigations.

The silver and lead salts (VII, Me = Ag, Pb) are also yellow and are formed in an acid medium. The silver salt is photosensitive and undergoes gradual decomposition with liberation of free silver.

Addition of organic bases to indandione sulfonic acid solution readily gives indandione sulfonates of these bases. The aniline, pyridine and quinoline salts thus obtained are colorless crystalline substances, very water-soluble; they are insoluble in alcohol and other organic solvents. They may be recrystallized from dilute ethanol.

Like other sulfonic acids [5], indandione sulfonic acid gives benzylthiouronium salt (VIII) with S-benzylthiourea; this salt crystallizes well and may be used for identification of indandione sulfonic acid.



(VIII)

Indandione sulfonic acid, unlike nitroindandione [6], forms enolic salts easily. Some of these, for example the lead salt (VII, Me = Pb), are formed even in acid solution (pH 5). The enolic salts are less soluble than the sulfonic acid salts (V, VII), and are therefore more easily isolated. Despite this, no enolic salts have as yet been obtained with organic bases.

EXPERIMENTAL

Indandione-1,3-sulfonic-2 acid (III). 6 g (0.025 mole) dioxane sulfotrioxide (D-SO_3), was added to 7.3 g (0.05 mole) indandione-1,3 in 70 ml 1,2-dichloroethane, with stirring and water cooling so as to prevent the temperature from rising above 25°. A dark red solution was formed and after 2-3 minutes solid began to separate out. After 1.5 hours the precipitate was filtered off with suction, washed with anhydrous dichloroethane and placed in a vacuum desiccator. Yield of indandione-1,3-sulfonic-2 acid 7 g, m. p. 85-90°, very readily soluble in water, alcohol, dioxane and acetone, insoluble in ether, chloroform and carbon tetrachloride.

Found %: S 12.40. $C_9H_6O_5S$. Calculated %: S 14.18.

Salts of indandionesulfonic acid with 1 equivalent of metal. The sodium, potassium, lithium and ammonium salts were obtained by diluting the reaction mixture after sulfonation with water, separating the dichloroethane in a separating funnel and salting out the aqueous solution by appropriate chlorides. The salts were recrystallized from dilute ethanol.

Sodium salt. Yellowish prisms. Two molecules of water of crystallization which are removed at 100-105°. The salt begins to decompose and char at 115-120°.

Found %: Na 8.01; S 11.40; H_2O 13.15. $C_9H_5O_5SNa \cdot 2H_2O$. Calculated %: Na 8.09; S 11.28; H_2O 12.67.

Potassium salt. Colorless prisms.

Found %: K 14.70; S 12.35. $C_9H_5O_5SK$. Calculated %: K 14.79; S 12.12.

Lithium salt. Pale yellow fine hexagonal prisms.

Found %: Li 2.98. $C_9H_5O_5SLi$. Calculated %: Li 2.71.

Ammonium salt. Colorless prisms.

Found %: N 5.54. $C_9H_5O_5SNH_4$. Calculated %: N 5.74.

Calcium salt (VI, Me = Ca) was obtained by addition of an alcoholic solution of calcium chloride to an alcoholic solution of indandione sulfonic acid. Yellowish bipyramids; crystallized with 2 molecules of water, removed slowly on drying at 100° for 12 hours. Decomposed at 115-120°. Very easily soluble in water.

Found %: Ca 7.64; H_2O 6.77. $(C_9H_5O_5S)_2Ca \cdot 2H_2O$. Calculated %: Ca 7.60; H_2O 6.84.

Strontium salt (VI, Me = Sr). Obtained by addition of aqueous solution of strontium bromide and a small amount of alcohol to an alcoholic solution of indandione sulfonic acid. Crystals began to appear after 15 minutes at 0°. Colorless prisms. Decomposed at 120°. Easily distinguished from the corresponding calcium salt under the microscope.

Found %: Sr 15.85. $(C_9H_5O_5S)_2Sr$. Calculated %: Sr 16.28.

Barium salt (VI, Me = Ba). Obtained in the same way as the calcium salt, but precipitation with alcohol not necessary. Colorless prisms, easily dissolved in water. Decomposed at 120°.

Found %: Ba 23.49. $(C_9H_5O_5S)_2Ba$. Calculated %: Ba 23.38.

Salts of indandione sulfonic acid with 2 equivalents of metal (V, VII). These salts were obtained by neutralization of an aqueous solution of indandione sulfonic acid with carbonates until an alkaline reaction was reached.

Sodium salt (V). Obtained as mentioned above and also by addition of sodium carbonate solution to an aqueous solution of the monosodium salt and precipitation with a small amount of ethanol. Recrystallization from dilute ethanol gave bright yellow prisms, easily soluble in water (giving a yellow coloration, which disappears on acidifying the solution).

Found %: Na 14.10; H_2O 16.55; S 9.85. $C_9H_4O_5SNa_2 \cdot 3H_2O$. Calculated %: Na 14.19; H_2O 16.65; S 9.87.

Potassium salt (V). Yellow prisms. Crystallized with 2 molecules of water.

Found %: K 23.10; H_2O 10.67. $C_9H_4O_5SK_2 \cdot 2H_2O$. Calculated %: K 23.10; H_2O 10.64.

Silver salt (V) obtained on addition of silver nitrate to an aqueous solution of indandione sulfonic acid. Recrystallized from dilute ethanol. Yellow prisms. Gradual decomposition on exposure to light.

Found %: Ag 49.30. $C_9H_4O_5SAg_2$. Calculated %: Ag 49.03.

Calcium salt (VII, Me = Ca). Obtained by addition of calcium carbonate to an aqueous solution of indandione sulfonic acid until alkaline reaction and precipitated from solution by a small amount of ethanol. Recrystallized from 70-80% ethanol. Long, fine yellow needles. Solubility in water at 20° 8.55 g/liter, but recrystallization from water unsuccessful.

Found %: Ca 15.19. $C_9H_4O_5SCa$. Calculated %: Ca 15.16.

Strontium salt (VII, Me = Sr). Prepared similarly to the calcium salt. Recrystallized from water with addition of a little ethanol. Long, fine lemon-yellow prisms. Crystallized with 3 molecules of water. Solubility in water at 20° 3.74 g/liter.

Found %: Sr 24.02; H_2O 14.50. $C_9H_4O_5SSr \cdot 3H_2O$. Calculated %: Sr 23.90; H_2O 14.77.

Barium salt (VII, Me = Ba). Prepared as the preceding salts. Precipitated out without addition of alcohol. Solubility in water: 1.04 g/liter at 20°. Crystallized in yellow prisms on evaporating down the solution. Crystals contained 3 molecules of water.

Found %: Ba 33.17; H_2O 12.63. $C_9H_4O_5SBa \cdot 3H_2O$. Calculated %: Ba 33.00; H_2O 12.95.

Magnesium salt (VII, Me = Mg). Obtained as the preceding salts. Recrystallized from dilute ethanol. Canary-yellow prisms, containing 5 molecules of water of crystallization. On drying the latter gradually removed, the last molecule at 160°.

Found %: Mg 7.21; H_2O 24.90. $C_9H_4O_5SMg \cdot 5H_2O$. Calculated %: Mg 7.18; H_2O 26.58.

Zinc salt (VII, Me = Zn). Recrystallized from dilute alcohol. Small tetrahedral orange-yellow prisms. Two molecules of water of crystallization, removed at 150°. Anhydrous salt lighter in color.

Found %: Zn 19.69; H_2O 11.18. $C_9H_4O_5SZn \cdot 2H_2O$. Calculated %: Zn 20.07; H_2O 11.06.

Cadmium salt (VII, Me = Cd). Recrystallized from water and a small amount of alcohol. Orange-yellow prisms. Crystallized with 2 molecules of water, removed at 150°. Anhydrous salt yellow.

Found %: Cd 29.85; H_2O 9.47. $C_9H_4O_5SCd \cdot 2H_2O$. Calculated %: Cd 30.17; H_2O 9.60.

Lead salt (VII, Me = Pb). Prepared from the monosodium salt and lead nitrate in aqueous solution. Precipitate dissolved in dilute nitric acid and the lead salt precipitated by neutralizing with ammonia to pH 5-6. Very slightly soluble in water. Yellow square plates.

Found %: Pb 48.40. $C_9H_4O_5SPb$. Calculated %: Pb 48.03.

Nickel salt (VII, Me = Ni). Prepared in the same way as the calcium salt. Recrystallized from dilute ethanol (1 : 1). Greenish-yellow very small prisms, 4 molecules of water of crystallization 2 of which (13.65%) were driven off at 105°, the remaining two at 150°.

Found %: Ni 15.87; S 8.76; H_2O 19.43. $C_9H_4O_5SNi \cdot 4H_2O$. Calculated %: Ni 16.53; S 9.02; H_2O 20.29.

Complex cobalt salt with pyridine. To an aqueous solution of indandione sulfonic acid was added cobalt carbonate until no more carbon dioxide was evolved. A brownish, water-insoluble precipitate was formed. Crystallization from very dilute pyridine gave long brownish-red crystals containing 2 molecules of pyridine and 1 molecule of water. A more convenient way of obtaining this complex consisted of addition to an aqueous solution of the monosodium salt of indandione sulfonic acid of cobalt nitrate and subsequent gradual addition of pyridine. Red crystals of the complex precipitated out immediately.

Found %: Co 12.12; N 6.14; S 6.97. $C_9H_4O_5SCo \cdot 2C_5H_5N \cdot H_2O$. Calculated %: Co 12.85; N 6.18; S 6.99.

Complex manganese salt with pyridine. Prepared similarly to the cobalt complex. Recrystallized from dilute pyridine (1 : 4). Red prisms. On exposure to air pyridine gradually left the molecule and the color of the crystals changed to yellow.

Found %: N 6.47; Mn 11.95; S 7.03. $C_9H_4O_5SMn \cdot 2C_5H_5N \cdot H_2O$. Calculated %: N 6.15; Mn 12.10; S 7.04.

Aniline salt. Prepared by addition of aniline to an alcoholic solution of indandione sulfonic acid. Recrystallized from dilute ethanol. Long colorless prisms. M. p. 145-148° (decomp.).

Found %: N4.39. $C_{15}H_{13}O_5NS$. Calculated %: N 4.44.

Pyridine salt. Similar to the aniline salt. Long colorless prisms (from dilute ethanol). M. p. 210-211° (decomp.).

Found %: N 4.89. $C_{14}H_{11}O_5NS$. Calculated %: N 4.59.

Quinoline salt. Similar to the aniline salt. Long colorless prisms (from dilute alcohol). M. p. 214° (decomp.).

Found %: N 4.14. $C_{18}H_{13}O_5NS$. Calculated %: N 3.95.

Benzylthiouronium salt (VIII). Prepared from the sodium salt of indandione sulfonic acid and benzylthiourea in alcoholic solution. Colorless prisms (from dilute ethanol). M. p. 192-194°.

Found %: N 6.82. $C_{17}H_{15}O_5S_2N_2$. Calculated %: N 7.17.

SUMMARY

1. Sulfonation of indandione with 1,3-dioxane sulfotrioxide under certain conditions gives both indandionemonosulfonic acid and the disulfonic acid. Reaction mechanism for sulfonation of indandione is given.

2. Unlike 2-nitroindandione, indandionesulfonic acid undergoes enolization easily.

3. It has been established that either the sulfo group alone or the sulfo group and the enol group may participate in the formation of salts of indandionesulfonic acid. A series of salts of both types has been prepared.

4. The cobalt, nickel and manganese salts of indandionesulfonic acid give complex compounds with pyridine.

5. Indandionesulfonic acid may be identified by its S-benzylthiouronic salt.

LITERATURE CITED

[1] E. Iu. Gudrinietse, E. Ia. Dreimanis and G. Ia. Vanag, Proc. Acad. Sci. USSR, 110, 786 (1956).*

[2] W. Truce and C. Alfieri, J. Am. Chem. Soc. 72, 2740 (1950).

[3] V. N. Ufimtsev, J. Gen. Chem. 16, 1020 (1946).

[4] B. V. Tronov and R. I. Kharitonov, Works of the Chemical Inst. Acad. Sci. Kirghiz SSR, No. 6, 157 (1955).

[5] Reactions and Methods of Investigation of Organic Compounds,** Moscow-Leningrad, 1952.

[6] G. Vanag, Nitroindandione, Academy of Sciences of the Latvian SSR Press, 1954.**

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*Original Russian pagination. See C. B. Translation.

**In Russian.

REACTION OF HYDROGEN PEROXIDE WITH ALLYL ALCOHOL AND ACROLEIN IN THE PRESENCE OF TUNGSTIC ACID

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A number of investigations have recently been published in connection with the reaction of unsaturated compounds with hydrogen peroxide in the presence of catalysts. These have shown that hydrogen peroxide adds on across the double bonds [1-11].

Milas [1] and Waters [12] consider that hydroxyl radicals are formed in this reaction and it is these radicals which add on across the double bonds. These authors' hypothesis has not, however, been confirmed experimentally. Nor has the view held by Mugdan [10] been proved; he considers that the reaction between hydrogen peroxide and allyl alcohol in aqueous solution and in the presence of tungstic acid is an ionic reaction. Crigee's work [13] merits attention; he showed that the interaction of unsaturated compounds with hydrogen peroxide in the presence of osmium tetroxide proceeds by way of osmic acid esters, which he succeeded in isolating from the reaction products. The hydroxyl derivatives are obtained by saponification of these esters.

The present work is concerned with studies of the reaction between allyl alcohol or acrolein and hydrogen peroxide in the presence of tungstic acid. The following sequence of reactions appears to take place in the case of allyl alcohol: hydrogen peroxide forms pertungstic acid with tungstic acid, pertungstic acid reacts with allyl alcohol at the double bond forming a glycidic alcohol ($H_2WO_5 + CH_2=CH-CH_2OH \rightarrow CH_2(O)CH-CH_2OH + H_2WO_4$) which is then hydrated to glycerol.

With acrolein, hydrogen peroxide reacts (in the presence of tungstic acid) almost exclusively at the carbonyl group, forming mainly acrylic acid.

According to the data of an American patent held by the Shell Company [11] the reaction between acrolein and hydrogen peroxide follows a different course in the presence of osmic anhydride. Hydrogen peroxide adds on across the double bond forming glyceraldehyde.

Such a direction of reaction is, evidently, a particular case of conversions studied by Crigee and apparently also proceeds by way of appropriate esters of osmic acid which are subsequently saponified. No peracids are formed and with respect to the interaction with acrolein the following course of the reaction must be suggested

$$CH_2=CH-CHO + OsO_4 \rightarrow CH_2(O)-CH(O)-CHO \xrightarrow{2H_2O} CH_2OH-CHOH-CHO + H_2OsO_4$$

(OsO_2 bridging the two O atoms)

$$H_2OsO_4 + H_2O_2 \rightarrow OsO_4 + 2H_2O$$

In the presence of tungstic acid, however, pertungstic acid is evidently formed first and then oxidizes the acrolein carbonyl group

$$H_2O_2 + H_2WO_4 \longrightarrow H_2WO_5 + H_2O$$

$$CH_2{=}CH{-}CHO + H_2WO_5 \longrightarrow CH_2{=}CH{-}COOH + H_2WO_4$$

EXPERIMENTAL

Reaction of allyl alcohol with hydrogen peroxide in the presence of tungstic acid. To a 9% aqueous solution of allyl alcohol, warmed to 70°, was added with vigorous stirring perhydrol (10% excess over theoretical) in which tungstic acid (3% with respect to allyl alcohol) had been dissolved. The reaction products were analyzed for glycerol content by the Bertram method [14], for allyl alcohol by the bromide-bromate method, for hydrogen peroxide iodometrically and for oxides by the Deckert-Lubatti method [15].

During the first 10-15 minutes after mixing the reagents, the reaction mixture contained up to 2% (calculated for glycidic alcohol) of compounds containing the oxide group. Their amount gradually decreased and after 3 hours reached 0.05%. In order to isolate the glycidic alcohol the reaction mixture was cooled soon after mixing the reagents and treated repeatedly with ether. The solvent was distilled off and the residue vacuum-distilled.

B. p. 65-70° (2.5 mm), d_4^{20} 1.119, n_D^{20} 1.4350.

Literature data: d_4^{20} 1.115, n_D^{20} 1.4302 [16].

Found %: C 48.98; H 7.90. $C_3H_6O_2$. Calculated %: C 48.65; H 8.17.

The insufficient purity of the isolated glycidol is explained by certain difficulties in isolating it from the mixture in which it is present in small concentration and the ease with which it is hydrated at raised temperatures. Hydration takes place very slowly at room temperature, but becomes rapid at 70°. This evidently provides the rationale for hydroxylation of allyl alcohol with hydrogen peroxide in the presence of tungstic acid at a temperature of 70°.

Glycerol was isolated from the reaction mixture by distilling off water and fractionating the residue under vacuum. Tungstic acid was first removed from solution by passage through anion-exchange resins. Glycerol was obtained in concentration of 99.3%.

A small amount of carbonyl compounds is formed as a side product in this reaction; this is evidently racemic glyceraldehyde which can be formed by oxidation of glycerol with hydrogen peroxide (especially in the presence of traces of iron oxide).

Analysis of the precipitate of dinitrophenylhydrazone isolated on treating the reaction mixture with 2,4-dinitrophenylhydrazine solution gave the following results:

Found %: C 39.02; H 3.70; N 20.80. $C_9H_{10}O_6N_4$. Calculated %: C 40.00; H 3.70; N 20.74.

The possibility is not, however, excluded that a certain amount of isomeric dihydroxyacetone is formed.

The yield of glycerol reaches 95% (calculated on allyl alcohol), the amount of carbonyl side products from 3 to 5%.

Reaction between acrolein and hydrogen peroxide in the presence of tungstic acid. To a 10% aqueous solution of acrolein at 70° perhydrol (10% excess over theoretical) in which tungstic acid (3% with respect to acrolein) had been dissolved was added with vigorous stirring. The reaction mixture was maintained at this temperature for 2 hours; acrolein and water were then distilled off from the reaction products. Acrylic acid was determined in the residue with reference to two functional groups: double bond by the bromide-bromate method and carbonyl group by titration with 0.1 N solution of sodium hydroxide in the presence of phenolphthalein; the content of carbonyl compounds was determined by precipitation with dinitrophenylhydrazine (calculated for glyceraldehyde).

The main reaction product was acrylic acid whose yield exceeded 70% calculated on acrolein; only 1-2% carbonyl compounds was formed.

The results of one of the experiments are given below.

Acrolein taken (g)	Residue after distillation of most of the water (g)	Results of residue analysis (%)		Yield calculated on acrolein (%)	
		acrylic acid	carbonyl compounds	acrylic acid	carbonyl compounds
22.5	43.3	50.4* 49.8**	1.3	76.7	1.7

*Bromide-bromate method

**Titration with 0.1 N NaOH

SUMMARY

1. A study was made of the interaction of hydrogen peroxide with allyl alcohol and acrolein in the presence of tungstic acid.

2. Precise data have been obtained on the sequence of events in these reactions.

LITERATURE CITED

[1] Milas, J. Am. Chem. Soc. 58, 1302 (1936).

[2] Milas, J. Am. Chem. Soc. 59, 2345 (1937).

[3] Milas, J. Am. Chem. Soc. 61, 1845 (1939).

[4] Milas, J. Am. Chem. Soc. 62, 1841 (1940).

[5] Dupont, Compt. rend. 203, 92 (1936).

[6] Treibs, Brennstoff-Chemie 20, 358 (1939).

[7] Treibs, Ber. 72, 137 (1939).

[8] Waters, Nature 158, 380 (1946).

[9] Taylor, Industrial Chemistry and Chemical Manufacturing, 9 (1953).

[10] Mugdan, J. Chem. Soc. 1949, 2988.

[11] U. S. Patent 2718529; Industrie chim. Belge, 21, 623 (1956).

[12] Waters, Chemistry of Free Radicals, Oxford, 246 (1944).

[13] Criegee, Lieb. Ann. 522, 755 (1936).

[14] Bertram, Rec. trav. chim. 57, 681 (1938).

[15] P. V. Zimakov, Ethylene Oxide,* Goskhimizdat, 1946.

[16] Dictionary of Organic Compounds,** Vol. II, 125.

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SYNTHESIS OF QUINUCLIDINE-3-ACETIC ACID

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In recent years a large number of mono- and disubstituted derivatives of quinuclidine have been obtained. Some of these compounds have shown important biologic properties. The main starting materials for the preparation of substituted derivatives of quinuclidine have been various quinuclidine carboxylic acids. The presence of carboxylic groups in these compounds permitted preparation of compounds not previously known for the quinuclidine series: aldehydes [1], amino acids, urethanes [2], lactones [3], various substituted amines [4] etc.

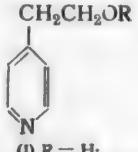
The compounds mentioned belong chiefly to 2-monosubstituted, 2,3- and 2,5 disubstituted derivatives of quinuclidine. Substituted quinuclidines with the substituents in position 3 have received less detailed study. In connection with this, the work of Lukes et al. [5] should be mentioned, since he studied preparation of 3-vinylquinuclidine, as well as work concerned with the synthesis of esters of quinuclidineol-3 [6] and quinuclidine-3-carboxylic acid [7].

The present work deals with the synthesis of quinuclidine-3-acetic acid which provides the opportunity for extending the investigation of 3-substituted derivatives of quinuclidine.

The starting material for the synthesis of quinuclidine-3-acetic acid was 4-(β-hydroxyethyl)-pyridine. This compound was obtained by condensation of a mixture of β- and γ-picolines with formaldehyde. 4-(β-hydroxyethyl)-pyridine was separated from the γ-di- and trimethylelpicolines formed at the same time by twice repeated vacuum distillation rather than by recrystallization of the picrate as proposed by Meisenheimer [8]. The yield of 4-(β-hydroxyethyl)-pyridine was 6-7% as against 1.2-1.5% shown by that author.

In order to carry out the proposed synthesis of quinuclidine-3-acetic acid it was necessary to effect the condensation of 4-(β-hydroxyethyl)-pyridine with chloral so as to obtain 1,1,1-trichloro-2-hydroxy-(pyridyl-4')-4-hydroxybutane. This condensation resulted in tarry products only, apparently as the result of formation not only of the addition product of chloral and 4-(β-hydroxyethyl)-pyridine but also of easily polymerized 4-vinylpyridine. It was proposed to replace the exceedingly reactive 4-(β-hydroxyethyl)-pyridine by acetoxy or benzoxy derivatives in which the ester group could be easily eliminated in the course of the synthesis.

4-(β-acetoxyethyl)-pyridine (II) was obtained with an 83% yield on treating 4-(β-hydroxyethyl)-pyridine (I) with acetyl chloride in 10 times the volume of pyridine at a temperature not exceeding 10°.

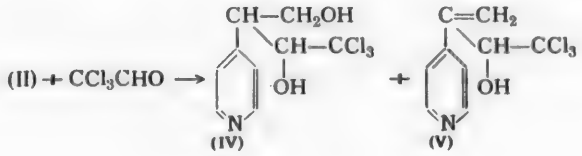


(I) R = H;
(II) R = $COCH_3$;
(III) R = COC_6H_5.

Halving the amount of pyridine or its replacement by benzene lowered the yield of the acetoxy derivative by 50%. Acetylation of 4-(β-hydroxyethyl)-pyridine with acetyl chloride at a temperature above 10°,

as well as by acetic anhydride, led to the formation of considerable amounts of 4-vinylpyridine. 4-(β-acetoxyethyl)-pyridine gradually turns viscous and brown when allowed to stand at room temperature. These phenomena are explained by conversion of the acetoxy derivative into 4-vinylpyridine which tends to polymerize and darken with time.

Condensation of 4-(β-acetoxyethyl)-pyridine (II) with chloral in benzene in the presence of piperidine acetate gave 1,1,1-trichloro-3-(pyridyl-4')-2,4-dihydroxybutane (IV) with a yield of about 10%. In addition to this substance an approximately equal amount of 1,1,1-trichloro-2-hydroxy-3-(pyridyl-4')-butene-4 (V) was isolated.

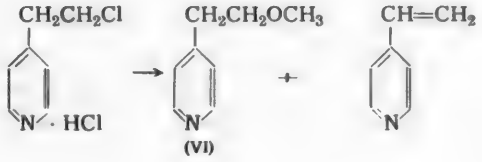


More prolonged heating of the reaction mixture (30 hours instead of 16 hours) leads to the exclusive formation of compound (V) with a yield of 30%. Condensation of (II) with chloral was also effected with pyridine and toluene as solvents, but only the unsaturated compound (V) was isolated in these cases.

4-(β-benzoxyethyl)-pyridine (III), obtained by interaction of 4-(β-hydroxyethyl)-pyridine with benzoyl chloride in aqueous alkali solution, decomposed on vacuum distillation with the formation of 4-vinylpyridine; consequently compound (III) was obtained in the pure state only in the form of the hydrochloride.

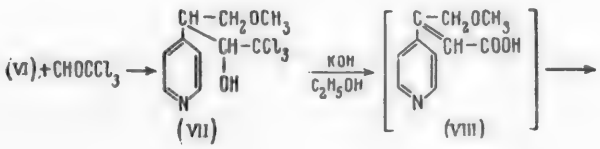
The data presented show that 4-(β-hydroxyethyl)-pyridine and its esters are easily converted into 4-vinylpyridine under the influence of such factors as time, temperature and chemical reagents.

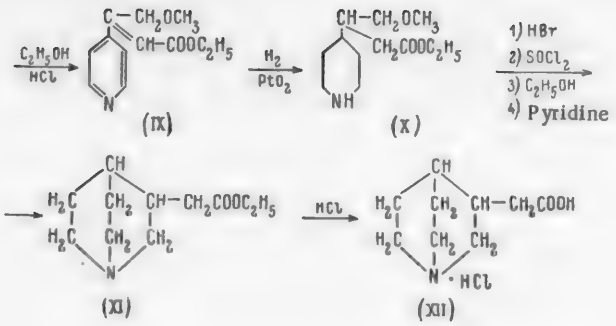
A more stable compound was found in 4-(β-methoxyethyl)-pyridine (VI). The latter was obtained by brief heating of 4-(β-chloroethyl)-pyridine hydrochloride with sodium methylate, the yield being 42%. In addition to compound (VI) a certain amount (11%) of 4-vinylpyridine was also formed.



Separation of these substances was easily achieved by fractional distillation under vacuum.

Conversion of 4-(β-methoxyethyl)-pyridine to quinuclidine-3-acetic acid was effected according to the following scheme.





4-(β-methoxyethyl)-pyridine was condensed with chloral in the presence of piperidine acetate; 1,1,1-trichloro-2-hydroxy-3-(pyridyl-4')-4-methoxybutane (VII) was obtained. In this case, unlike the analogous reaction of 4-(β-acetoxyethyl)-pyridine with chloral, no formation of substituted 4-vinylpyridine was observed.

Compound (VII) was treated with an alcoholic solution of potassium hydroxide, the 4-methoxy-3-(pyridyl-4')-crotonic acid (VIII) formed was converted directly into the ethyl ester (IX). Reduction of pyridylcrotonic ester (IX) in the presence of platinum catalyst (according to Adams) at room temperature gave the ethyl ester of 4-methoxy-3-(piperidyl-4')-butyric acid (X). In order to replace the methoxy group by halogen and to obtain the quinuclidine derivative, compound (X) was heated with 67% hydrobromic acid in a sealed tube at 110-120°. The 4-bromo-3-(piperidyl-4')-butyric acid thus formed was esterified and then subjected to cyclization in the presence of pyridine, giving the ethyl ester of quinuclidine-3-acetic acid (XI). Saponification of the latter gave quinuclidine-3-acetic acid (XII).

EXPERIMENTAL

4-(β-hydroxyethyl)-pyridine (I). 806 g of a mixture of β- and γ-picolines, 180 g formalin (approximately 40%) and 700 ml water were boiled for 16 hours. β-Picoline and unreacted γ-picoline and formaldehyde were removed by steam-distillation. The reaction liquid was evaporated down under vacuum to the remaining thick liquid consisting of 4-(β-hydroxyethyl)-pyridine and small amounts of γ-di- and trimethylolpicolines, was added a mixture of 200 ml ether and 200 ml chloroform. After 3-5 hours the ether-chloroform solution was poured off from the undissolved residue, containing tarry substances and γ-trimethylolpicoline, and dried over sodium sulfate. After distilling off the solvents the residue was vacuum distilled. Twice repeated distillation yielded 29.6 g (6.5% taking the mixture to contain 40% γ-picoline) 4-(β-hydroxyethyl)-pyridine. B. p. 140-141° (9 mm). Picrate m. p. 132.5-134° [8].

4-(β-acetoxyethyl)-pyridine (II). To a solution of 4 g 4-(β-hydroxyethyl)-pyridine in 40 ml anhydrous pyridine was added with stirring 2.82 g acetyl chloride. The temperature was maintained within the range 0-10°. After the addition of acetyl chloride the reaction mixture was stirred at this temperature for a further 1½ hours. 20 ml water and 40 ml 15% soda solution was then added and the mixture extracted with benzene. The benzene solution was dried over potassium carbonate, the solvent distilled off and the residue vacuum-distilled. Yield 4.5 g (83.8%). Colorless mobile liquid, easily soluble in organic solvents, with difficulty in water. B. p. 124° (8 mm), n_D^{18} 1.5022.

Found %: C 65.64; H 6.67; N 8.50. $C_9H_{11}O_2N$. Calculated %: C 65.50; H 6.67; N 8.49.

Hydrochloride – colorless crystals, m. p. 98-100°. At 117° the molten substance became cloudy, then solidified and melted at 238° (melting point of 4-vinylpyridine hydrochloride). Thus, on heating, hydrochloride (II) was converted into 4-vinylpyridine hydrochloride.

4-(β-benzoxyethyl)-pyridine (III). To a solution of 5 g 4-(β-hydroxyethyl)-pyridine in 12 ml of water was added 6.1 ml 40% aqueous solution of sodium hydroxide and then, with stirring, 6.9 g benzoyl chloride. After mixing the components, the reaction mixture was stirred for 1 hour and extracted with ether. The ethereal solution was dried over potassium carbonate, filtered and treated with 20% alcoholic solution of hydrogen chloride until an acid reaction to Congo. The crystals which separated out were filtered off, washed with ether and dried. Yield 6.4 g (60%) 4-(β-benzoxyethyl)-pyridine hydrochloride. Colorless crystals, easily soluble in water and alcohol, insoluble in ether, acetone. M. p. 121-123° (from a mixture of alcohol and ether).

Found %: N 5.76. $C_{14}H_{13}O_2N \cdot HCl$. Calculated %: N 5.32.

Condensation of 4-(β-acetoxyethyl)-pyridine with chloral. a) To a solution of 2.4 g 4-(β-acetoxyethyl)-pyridine and 2.1 g chloral in 15 ml anhydrous benzene was added 8 drops of piperidine and 6 drops of glacial acetic acid. The reaction mixture was heated at 80° for 16 hours; the mixture gradually turned a dark brownish color. On cessation of heating the benzene was distilled off under vacuum, the residue dissolved in 12 ml 7% hydrochloric acid and boiled for 10 minutes. The hydrochloric acid solution was cooled and treated with soda until an alkaline reaction to phenolphthalein; a large amount of tar separated out at this stage. The alkaline solution was extracted with benzene, the benzene solution dried over potassium carbonate, the solvent distilled off under vacuum and the remaining oily crystals triturated with ether. The crystals which separated out were filtered off, washed with ether and recrystallized from benzene. Yield 0.4 g (10%) 1,1,1-trichloro-3-(pyridyl-4')-2,4-dihydroxybutane (IV). Colorless crystals, easily soluble in chloroform, less so in ethyl acetate, benzene, acetone, alcohol, insoluble in water and in ether. M. p. 117-119°.

Found %: C 40.17; H 3.83; N 5.22; Cl 38.74. $C_9H_{10}O_2NCl_3$. Calculated %: C 39.93; H 3.70; N 5.17; Cl 39.20.

The ethereal mother liquor left after separation of crystals (IV) was treated with 20% alcoholic solution of hydrogen chloride until an acid reaction to Congo. The oil which separated out was washed by decantation with ether and triturated with a small amount of anhydrous alcohol. 0.4 g 1,1,1-trichloro-2-hydroxy-3-(pyridyl-4')-butene-4-hydrochloride (V) separated out. Colorless crystals, easily soluble in water and alcohol, insoluble in ether, acetone, benzene. M. p. 153-154° (decomp.) from a mixture of alcohol and ether.

Found %: C 37.49; H 3.12; N 5.04; Cl' 12.14. $C_9H_8ONCl_3 \cdot HCl$. Calculated %: C 37.38; H 3.11; N 4.85; Cl' 12.27.

b) 8.35 g 4-(β-acetoxyethyl)-pyridine, 7.37 g chloral, 0.48 ml piperidine and 0.24 ml glacial acetic acid were heated at 80° for 30 hours. After treatment similar to that described in the preceding experiment, the benzene extract yielded 3.75 g (29.4%) 1,1,1-trichloro-2-hydroxy-3-(pyridyl-4')-butene-4 (V). Colorless crystals, easily soluble in benzene, acetone, alcohol, insoluble in water and in ether. M. p. 128-129° (from benzene).

Found %: C 42.43; H 3.18; N 5.50; Cl 42.24. C_9H_8ONCl. Calculated %: C 42.77; H 3.17; N 5.54; Cl 42.24.

4-(β-methoxyethyl)-pyridine (VI). To an alcoholic solution of sodium methylate, obtained from 33 g sodium and 260 ml anhydrous methyl alcohol, was added with cooling a solution of 28 g 4-(β-chloroethyl)-pyridine hydrochloride in 200 ml anhydrous methyl alcohol. The reaction mixture was boiled for 1 hour; the solution, which was green when the components were mixed, turned a brownish color. After cooling, methyl alcohol saturated with hydrogen chloride was added to the reaction mixture until an acid reaction to Congo. The sodium chloride which precipitated out was filtered off and the alcoholic solution evaporated down under vacuum. The residue was dissolved in 30 ml water, 100 ml 15% soda solution added to it and the whole extracted with ether. The ethereal solution was dried over potassium carbonate, the ether distilled off and the residue distilled under vacuum at 8 mm. Two fractions were collected: 1st fraction, b. p. 65-80° (1.87 g) contained mainly 4-vinylpyridine; 2nd fraction, b. p. 80-92° (12.3 g) consisted of 4-(β-methoxyethyl)-pyridine and a small amount of 4-vinylpyridine. When the 2nd fraction was fractionated repeatedly 9.2 g (42.6%)

4-(β -methoxyethyl)-pyridine was obtained. B. p. 92-93° (10 mm). Colorless, mobile liquid, easily soluble in organic solvents, insoluble in water.

Found %: N 10.29. $C_8H_{11}ON$. Calculated %: N 10.22.

Picrate – yellow crystalline powder, easily soluble in acetone, alcohol, insoluble in water, ether. M. p. 93-95° (from alcohol).

Found %: C 46.27; H 4.21; N 15.28. $C_8H_{11}ON \cdot C_6H_3O_7N_3$. Calculated %: C 45.90; H 3.82; N 15.30.

1,1,1-Trichloro-2-hydroxy-3-(pyridyl-4')-4-methoxybutane (VII). 23.4 g 4-(β -methoxyethyl)-pyridine, 25.2 g chloral, 1.5 g piperidine and 0.8 ml glacial acetic acid were heated at 50-55° (in a water bath) for 29 hours. The reaction mixture was cooled, diluted with ethyl acetate, the crystals which separated out were filtered off and washed on the filter with anhydrous alcohol. Yield 1,1,1-trichloro-2-hydroxy-3-(pyridyl-4')-4-methoxybutane 10.7 g [46.3% calculated on reacted 4-(β -methoxyethyl)-pyridine]. Colorless crystals, moderately soluble in alcohol, poorly soluble in ethyl acetate, insoluble in ether, water. M. p. 172° (from alcohol).

Found %: C 42.13; H 4.51; N 4.79; Cl 37.70. $C_{10}H_{12}O_2NCl_3$. Calculated %: C 42.18; H 4.22; N 4.92; Cl 37.43.

The ethyl acetate mother liquor was evaporated down under vacuum, the residue dissolved in ether, the ethereal solution filtered from tarry substances and dried with potassium carbonate. After the ether was distilled off, the substance was vacuum distilled. 12.3 g of original 4-(β -methoxyethyl)-pyridine was recovered.

Ethyl ester of 3-(pyridyl-4')-4-methoxycrotonic acid (IX). To a solution of 10.7 g potassium hydroxide in 210 ml anhydrous alcohol was added 9 g 1,1,1-trichloro-2-hydroxy-3-(pyridyl-4')-4-methoxybutane. The reaction mixture became homogeneous in the course of 1 hour; after an additional time, potassium chloride began to precipitate out from the solution. The reaction mixture was allowed to stand at room temperature for 15 hours; it was then heated for 2 hours at 40-50°, after which excess potassium hydroxide was precipitated by means of carbonic acid in the form of potassium bicarbonate. Inorganic salts were separated, alcohol distilled off under vacuum and 20 ml 7% alcoholic solution of hydrogen chloride was added to the residue and the whole boiled for 3 hours. Alcohol was then distilled off under vacuum, the residue treated with 20 ml 50% solution of potassium carbonate and extracted with ether. The ethereal solution was dried over potassium carbonate and after the ether was distilled off, the product was vacuum distilled. 4.4 g (63%) ethyl ester of 3-(pyridyl-4')-4-methoxycrotonic acid was obtained. Colorless, mobile liquid, easily soluble in organic solvents, insoluble in water. B. p. 118-119° (0.1 mm).

Found %: C 65.43; H 6.94; N 6.35. $C_{12}H_{15}O_3N$. Calculated %: C 65.16; H 6.78; N 6.33.

Ethyl ester of 3-(piperidyl-4')-4-methoxybutyric acid (X). To a solution of 6.32 g ethyl ester of 3-(pyridyl-4')-4-methoxycrotonic acid in 60 ml anhydrous alcohol was added alcoholic solution of hydrogen chloride, containing 1.04 g hydrogen chloride, and 0.3 g platinum oxide. The reaction mixture was shaken with hydrogen at room temperature until the requisite amount of hydrogen (2870 ml) had been absorbed. The platinum black was then filtered off and the alcoholic solution evaporated down under vacuum. The hydrochloride of the ethyl ester of 4-methoxy-3-(piperidyl-4')-butyric acid was obtained in the form of a noncrystallizing oil. Yield quantitative.

The hydrochloride of the ester was treated with an aqueous solution of potassium carbonate and converted to the base. B. p. 105-108° (0.1 mm). Colorless liquid, easily soluble in organic solvents, poorly in water.

Found %: C 62.23; H 10.10; N 6.00. $C_{12}H_{23}O_3N$. Calculated %: C 62.88; H 10.00; N 6.12.

Ethyl ester of quinuclidine-3-acetic acid (XI). 1.2 g hydrochloride of the ethyl ester of 3-(piperidyl-4')-4-methoxybutyric acid and 20 ml 67% hydrobromic acid were heated in a sealed tube at 110-120° for 12 hours.

evaporated down under vacuum. The residue was dried by thrice-repeated addition of benzene with subsequent vacuum distillation. The 3-(piperidyl-4')-4-bromobutyric acid hydrobromide was heated with 7 ml thionyl chloride for 6 hours at 60-65°. Excess thionyl chloride was then distilled off under reduced pressure; the chloroanhydride obtained was heated with 7 ml anhydrous alcohol for 3 hours. After the alcohol was distilled off, the ester hydrochloride was treated with 50% solution of potassium carbonate and the base extracted with ether. The ethereal solution was dried with potassium carbonate, the ether was removed and the residue treated by boiling with 5 ml pyridine for 2 hours. Pyridine was then distilled off under vacuum; the residue was treated with 4 ml 25% solution of potassium carbonate and extracted with ether. After the ether had been removed, the product was vacuum distilled twice. Yield 0.24 g (27%). Colorless, mobile liquid, readily soluble in water and organic solvents. B. p. 91-93° (0.15 mm).

Found %: N 7.29; 7.21. $C_{11}H_{19}O_2N$. Calculated %: N 7.11.

Quinuclidine-3-acetic acid. 0.12 g ethyl ester of quinuclidine-3-acetic acid and 2 ml 18% hydrochloric acid were boiled for 5 hours. The acid solution was decolorized with animal charcoal and evaporated down under vacuum. The oily crystals obtained were triturated with acetone, the precipitate filtered off, washed with anhydrous alcohol and recrystallized from a mixture of alcohol and ether. Colorless crystals, easily soluble in water, soluble in alcohol on heating, insoluble in ether, acetone. M. p. 238° (decomp.).

Found %: C 51.93; H 7.63. $C_9H_{15}O_2N \cdot HCl$. Calculated %: C 52.60; H 7.77.

SUMMARY

1. Quinuclidine-3-acetic acid was synthetized from 4-(β-hydroxyethyl)-pyridine by way of 4-(β-methoxyethyl)-pyridine, 1,1,1-trichloro-2-hydroxy-3-(pyridyl-4')-4-methoxybutane, ethyl ester of 4-methoxy-3-(pyridyl-4')-crotonic acid and ethyl ester of 4-methoxy-3-(piperidyl-4')-butyric acid.

2. Certain ethers and esters of 4-(β-hydroxyethyl)-pyridine were obtained. It was shown that 4-(β-hydroxyethyl)-pyridine and its esters were readily converted to 4-vinylpyridine under the influence of such factors as time, temperature, chemical reagents. 4-(β-methoxyethyl)-pyridine proved to be a much more stable compound.

LITERATURE CITED

[1] M. V. Rubtsov and L. N. Iakhontov, J. Gen. Chem. 25, 2143 (1955).*

[2] M. V. Rubtsov and E. E. Mikhlina, J. Gen. Chem. 26, 135 (1956).*

[3] E. E. Mikhlina and M. V. Rubtsov, J. Gen. Chem. 27, 691 (1957).*

[4] M. V. Rubtsov, E. S. Nikitskaia, E. E. Mikhlina, A. D. Ianina and V. Ia. Furshtatova, J. Gen. Chem. 23, 1555 (1953);* M. V. Rubtsov, E. E. Mikhlina and V. Ia. Furshtatova, J. Gen. Chem. 24, 2217 (1954).*

[5] R. Lukes, Coll. Czechosl. Chem. 14, 655, 665 (1949); R. Lukes and I. Ernest, Coll. Czechosl. Chem. 15, 150 (1950); I. Ernest, Coll. Czechosl. Chem. 15, 322, 486 (1950).

[6] L. Sternbach and S. Kelser, J. Am. Chem. Soc. 74, 2215, 2219 (1952).

[7] C. A. Grob and E. Renk, Helv. Chim. Acta 37, 1689 (1954).

[8] J. Meisenheimer, Lieb. Ann. 420, 205 (1920).

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HYDROGENATION IN THE PRESENCE OF COLLOIDAL PALLADIUM

IX. HYDROGENATION OF VINYLPROPYL- AND VINYLBUTYLACETYLENES

Kh. V. Bal'ian, Z. A. Lerman and L. A. Merkur'eva

In work carried out with the participation of one of us [1], a study was made of the hydrogenation of two homologs of vinylacetylene, viz. vinylmethyl- and vinylethylacetylene. It appeared interesting to investigate the hydrogenation of other substituted vinylacetylenes containing radicals with longer carbon chains.

With this aim in view, we investigated hydrogenation of two hydrocarbons – vinylpropyl- and vinylbutylacetylene – in the presence of colloidal palladium with and without addition of decelerator (p-thiocyanochlorobenzene).

The hydrogenation products were separated from the original hydrocarbon and the mixture of olefins and diolefins obtained was brominated. The bromides formed were separated by vacuum distillation into di- and tetrabromides. The ratio of olefins to diolefins formed during hydrogenation was judged by the amounts of di- and tetrabromides obtained.

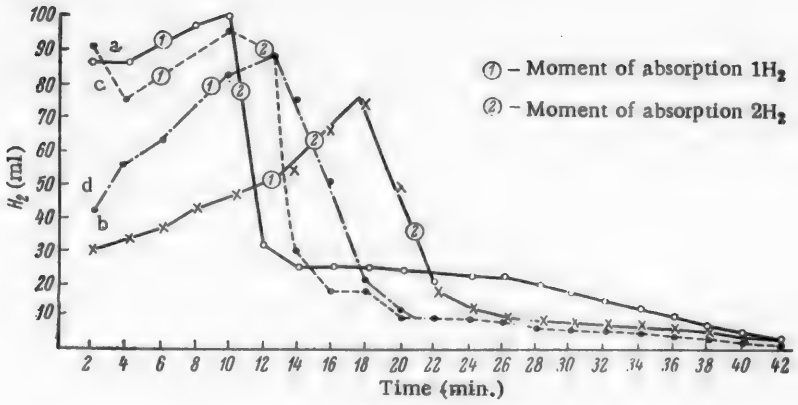
The olefins and diolefins were regenerated from the bromides by treatment with zinc in aqueous alcohol solution. Their structure was determined from physical constants, results of ozonolysis and condensation determined from physical constants, results of ozonolysis and condensation with maleic anhydride. It was found that the hydrocarbons under investigation differed little from their homologs – vinylmethyl and vinylethylacetylene [1] – studied earlier, with respect to the character of the curve for the rate of hydrogenation (see Fig.), site of initial addition of hydrogen, relative ease of addition of the first two molecules of hydrogen and the sharp drop in the rate of addition of the third molecule of hydrogen.

Formation of three hydrocarbons could be expected to result from the addition of one molecule of hydrogen to vinylalkylacetylene:

$R-CH=CH-CH=CH_2$ (I)
$R-C\equiv C-CH_2-CH_3$ (II)
$R-CH=C=CH-CH_3$ (III) R = n-C_3H_7 or n-C_4H_9.

As in the previous cases, when R = CH_3 or C_2H_5, no hydrocarbons (II) and (III) were found. In addition to hydrocarbon (I) olefins were found which were formed during further hydrogenation of the alkadiene hydrocarbon. Hydrogenation of vinylpropylacetylene thus gave heptadiene-1,3 and a mixture of heptenes (chiefly heptene-1 and heptene-2) in the approximate ratio of 1 : 1.6. The same hydrocarbons were also obtained on hydrogenation of vinylpropylacetylene in the presence of p-thiocyanochlorobenzene (0.014% calculated on the weight of hydrocarbon), but, together with some slowing of the process (see Fig.) there was some change in the ratio between diene and olefin (1 : 0.94). This change indicated that the decelerator increased somewhat the selectivity of the hydrogenation process, by slowing the further conversion of diene into olefins.

When vinylbutylacetylene was hydrogenated with a ratio of 1 mole hydrocarbon : 1 mole hydrogen, octadiene-1,3 and a mixture of octenes were obtained in the ratio 1 : 1. The same hydrocarbons but in a ratio of



Catalytic hydrogenation of vinylbutylacetylene and vinylpropylacetylene.
a) Vinylbutylacetylene without decelerator; b) the same with decelerator;
c) vinylpropylacetylene without decelerator; d) the same with decelerator.

1.3 : 1 were obtained in the presence of p-thiocyanochlorobenzene amounting to 0.013% with respect to the weight of the hydrocarbon. It was noted that p-thiocyanochlorobenzene, amounting to 0.2% of the weight of the hydrocarbon, inhibited hydrogenation completely, acting as a catalyst poison; 0.1% of the decelerator caused very marked slowing of hydrogen addition, especially at the beginning of the process (Table 2). The positive effect of the decelerator on the selectivity of the hydrogenation process thus also manifested itself in the case of vinylbutylacetylene.

EXPERIMENTAL

Vinyl-n-propylacetylene (b. p. 108-109°, d_4^{20} 0.7654, n_D^{20} 1.4513) and vinyl-n-butylacetylene (b. p. 49-50° at 41-42 mm, 134-135° (760 mm) d_4^{20} 0.7749, n_D^{20} 1.4551) were synthetized from vinylacetylene and the appropriate alkyl halide in the presence of metallic sodium and liquid ammonia• [2].

Preparation of colloidal palladium and electrolytic hydrogen and description of the hydrogenation apparatus have been given earlier [3].

Hydrogenation of vinylpropylacetylene. a) In order to discover the character of complete hydrogenation and the effect of decelerator on the rate of hydrogenation of vinylpropylacetylene, parallel experiments were performed in which 1 g hydrocarbon, 2 ml (2 mg) Pd and 40 ml methanol were used without decelerator and with 0.4 mg (2 ml alcoholic solution) of p-thiocyanochlorobenzene at 17° and 765 mm. 753 ml was calculated for $3H_2$. Some slowing of the process caused by addition of p-thiocyanochlorobenzene•• could be seen from comparison of curves (c and d in Fig.) plotted with time in minutes along the abscissa and amount of hydrogen absorbed in milliliters during equal periods of time along the ordinate. In the experiment without decelerator, 67% hydrogen ($2H_2$) added on during 12 minutes; with decelerator the same amount was taken up during 15 minutes. After this in both cases the rate of hydrogenation showed a marked fall. In the former case 96% hydrogen was absorbed in 72 minutes; in the latter only 93% hydrogen was absorbed in 108 minutes.

b) Vinylpropylacetylene was hydrogenated in the ratio 1 mole hydrocarbon : 1 mole hydrogen. 13.5 g hydrocarbon, 4 ml (4 mg) Pd, 175 ml methanol (18°, 787 mm) were taken. The calculated amount of 2H (3340 ml) added on during 51 minutes. 12 g hydrocarbon (88.8%) was isolated from the reaction mixture.

•Synthesis of vinylpropylacetylene from propyl chloride gives a small yield (about 20%), whereas with propyl bromide the yield is 55-60%. Propyl bromide (b. p. 70-72°, d_4^{20} 1.3426, n_D^{20} 1.4330) was obtained from propyl acetate, H_2SO_4 (d 1.84) and potassium bromide with a yield of 60%.

••The corresponding tables with numerical data are omitted for purposes of space economy.

The following fractions were obtained on distillation with a fractionating column:

1st fraction 96-100°, 4.4 g, n_D^{20} 1.4174, d_4^{20} 0.7112; 2nd 100-104°, 3.2 g, n_D^{20} 1.4268, d_4^{20} 0.7279; residue 2.5 g, n_D^{20} 1.4516, d_4^{20} 0.7628.

The residue (25%) was seen to be the original hydrocarbon from its constants and was not subjected to further studies. For better separation of olefins from diolefins, the 1st and 2nd fractions (7.6 g) were brominated with 8 ml bromine in 40 ml chloroform. After distilling off chloroform with a water-pump the liquid bromides obtained were distilled twice at 4 mm. Two fractions were thus obtained:

1st 75-76°, 5.3 g, n_D^{20} 1.5030, d_4^{20} 1.5146; 2nd 133-134°, 5.4 g, n_D^{20} 1.5790, d_4^{20} 2.0958.

1st fraction. Found %: Br 62.60. $C_7H_{14}Br_2$. Calculated %: Br 62.02.

2nd fraction. Found %: Br 76.40. $C_7H_{12}Br_4$. Calculated %: Br 76.90.

The amounts of di- and tetrabromides obtained showed that olefins and diolefins obtained as the result of complete hydrogenation of vinylpropylacetylene were in the ratio 1.6:1.

From 5.0 g dibromide, 1.6 g olefin (83%) was regenerated by zinc in aqueous alcohol solution; the olefin had b. p. 95°, n_D^{20} 1.4050, d_4^{20} 0.7039.

0.33 g olefin was subjected to ozonolysis; the ozonides were decomposed and heated with a solution of β-naphthol. 0.2264 g dinaphtholmethane was obtained, corresponding to 22.3% heptene-1. Another sample of the olefin hydrocarbon was also subjected to ozonolysis; the ozonides formed were decomposed, the products of ozonolysis oxidized with $KMnO_4$ and the acids obtained subjected to prolonged extraction with ether and drying with anhydrous Na_2SO_4. After distilling off the ether the acid residues (2.5 g) were fractionally distilled from a small flask at ordinary pressure and two fractions were collected: 1st 115-116° (0.8 g) and 2nd 166-167° (0.6 g). The first fraction consisted of acetic acid, the second of valeric acid.

Taking into account the results of ozonolysis and the constants of the olefin [4] and the dibromide [5], it may be concluded that incomplete hydrogenation of vinylpropylacetylene resulted in a mixture of heptene-1 and heptene-2.

Of 5.1 g tetrabromide 1.1 g (91%) diolefin with b. p. 102-104°, n_D^{20} 1.4412, d_4^{20} 0.7387 was regenerated by zinc in aqueous alcohol solution.

There are no data in the literature concerning 1,2,3,4-tetrabromoheptane. References to heptadiene-1,3 are difficult to check in the original: n_D^{20} 1.4493 and d_4^{20} 0.7152 are given without citing the boiling point. Karasaev [6] gives the following values for an equal mixture of heptadiene-1,3 and heptadiene-1,4: b. p. 97-104°, n_D^{20} 1.4419 and d_4^{20} 0.7331, and for heptadiene-1,4: b.p. 100-101.5°, n_D^{20} 1.4370 and d_4^{20} 0.7270. The latter hydrocarbon is characterized in another source [7] by widely divergent data: b. p. 92°, n_D^{20} 1.420, d_4^{20} 0.7176.

In our case the tetrabromide could be formed either from heptadiene-1,3 or heptene-3, but the latter is excluded as it has b. p. 105-106°, 106-107°, n_D^{20} 1.415, d_4^{20} 0.7337 [8].

The diene obtained by us was condensed with maleic anhydride. Condensation took place to the extent of 41%, evidently at the expense of the trans-isomer only: 0.60 g heptadiene, 0.750 g maleic anhydride and 12 ml xylene were heated for 4 hours at 110-120° in a sealed ampoule. Maleic anhydride which did not enter the reaction was converted to maleic acid by boiling with water [6] and the acid was titrated with 22.6 ml NaOH (0.47 N), which corresponded to 0.50 g maleic anhydride which did not enter the condensation.

In order to elucidate the influence of the decelerator on the composition of the products of hydrogenation of vinylpropylacetylene with a ratio 1 mole hydrocarbon : 1 mole hydrogen, 29 g hydrocarbon was taken with 8 ml (8 mg) Pd, 240 ml methanol and 2 ml alcoholic solution p-thiocyanochlorobenzene (4 mg). Hydrogenation was carried out at 17° and 765 mm. The amount of hydrogen calculated for 2H was 7300 ml and was absorbed in 72 minutes. After isolation, purification, drying and repeated distillations at ordinary pressure the following fractions were collected:

1st 96-100°, 12.3 g, n_D^{20} 1.4220, d_4^{20} 0.7108; 2nd 100-104°, 6.2 g, n_D^{20} 1.4310, d_4^{20} 0.7260; residue 1.8 g, n_D^{20} 1.4510, d_4^{20} 0.7624.

The residue corresponded to the original hydrocarbon. The 1st and 2nd fractions together (18.5 g) were brominated with 20 ml bromine in 200 ml chloroform. After the chloroform was distilled off the liquid bromides were subjected to repeated vacuum distillation at 2mm, giving the following fractions:

1st 72-74°, 17.8 g, n_D^{20} 1.5006, d_4^{20} 1.5166; 2nd 130-131°, 30.1 g, n_D^{20} 1.5784, d_4^{20} 2.0952.

From 17.5 g dibromide 5.4 g (82%) olefin, b. p. 94-95°, n_D^{20} 1.4050 and d_4^{20} 0.7028 was regenerated. From 30 g tetrabromide 5.7 g (84%) diolefin, b. p. 102-104°, n_D^{20} 1.4404, d_4^{20} 0.7374, was regenerated.

The fact that the constants coincided for the dibromides, tetrabromides, regenerated olefins and diolefins obtained on hydrogenation with and without decelerator obviated the need for further investigation of these regenerated hydrocarbons.

The ratio of olefins and diolefins was calculated from the amounts of di- and tetrabromides obtained on hydrogenation with decelerator. The ratio was 0.94 : 1; the decrease in olefin and unreacted (unhydrogenated) original hydrocarbon indicated that the addition of p-thiocyanochlorobenzene favored the addition of hydrogen to the triple bond and hindered the addition to the double bond of the diolefins.

Hydrogenation of vinyl-n-butylacetylene. a) In order to elucidate the nature of complete hydrogenation and the effect of substituent on the rate of hydrogenation of vinylbutylacetylene, parallel experiments were set up: 1.0619 g hydrocarbon, 2 ml (2 mg) Pd, 40 ml methanol and 1.0930 g hydrocarbon; 2 ml (2 mg) Pd, 40 ml methanol and 0.2 ml alcoholic solution of p-thiocyanochlorobenzene (0.4 mg),* in both cases at 22° and 750 mm. The amount of hydrogen calculated for the first experiment ($3H_2$ — 726 ml) was absorbed in 36 minutes, while in the second experiment only 85% hydrogen calculated for $3H_2$ (753 ml) was taken up in 90 minutes.

The effect of the decelerator can be seen by comparing curves a and b in the Figure.

b) Vinylbutylacetylene was hydrogenated in the ratio 1 mole hydrocarbon : 1 mole hydrogen at 18° and 787 mm. The results are given in Table 1.

TABLE 1

Expt.	Amount hydrocarbon (g)	Amount methanol (ml)	Amount colloidal Pd (ml)	Calculated 2H (ml)	Time (min.)
I	20.384	225	15 (15 mg)	4390	24
II	19.060	200	10 (10 mg)	4100	27

The reaction masses of the two experiments were combined and from this mixture was isolated 33.7 g (85.5%) crude product. After drying over fused $CaCl_2$ 31.6 g hydrocarbon was fractionally distilled at normal pressure and a fraction with b. p. 126-131°, n_D^{20} 1.4317, d_4^{20} 0.7428 was collected, amounting to 25.7 g. The residue in the distilling flask (3.8 g, 13%) had n_D^{20} 1.4596, d_4^{20} 0.7931, i.e., was apparently somewhat contaminated original hydrocarbon. It was not investigated further.

In order to separate the olefins from diolefins, 25.7 g of the product was brominated with 25 ml bromine in 125 ml chloroform. After distilling off the chloroform and repeated fractional distillations under vacuum (3-4 mm) two fractions were collected:

1st 83-84°, 21.8 g, n_D^{20} 1.4985, d_4^{20} 1.4586; 2nd 145-147°, 35.9 g, n_D^{20} 1.5722, d_4^{20} 1.9768.

1st fraction. Found %: Br 58.36. $C_8H_{16}Br_2$. Calculated %: Br 58.82.

2nd fraction. Found %: Br 74.43. $C_8H_{14}Br_4$. Calculated %: Br 74.41.

According to the di- and tetrabromides obtained, the calculated ratio between olefins and diolefins was approximately 1 : 1.

*Experiment with 1 ml solution of p-thiocyanochlorobenzene (2 mg) failed; no hydrogen was absorbed over a period of 40 minutes. With 0.5 ml p-thiocyanochlorobenzene (1 mg) hydrogen began to be absorbed only 20 minutes after the start of the experiment and only 75% of hydrogen calculated for $3H_2$ was taken up in the course of 153 minutes.

The tetrabromides yielded on freezing 5 g solid product with m. p. 66° (from methanol).

21 g dibromide, treated with zinc in aqueous alcohol solution, yielded 8.1 g (94%) hydrocarbon which gave on distillation at normal pressure 6 g hydrocarbon with b. p. 122-123°, n_D^{20} 1.4139, d_4^{20} 0.7244. Residue 1.4 g.

0.28 g olefin, after decomposition of its ozonides, gave with β-naphthol 0.2012 g dinaphtholmethane, which indicated the presence of about 26% octene-1 in the olefins. 3.8 g olefin was ozonized, the ozonides decomposed and the decomposition products converted to acids by oxidation with $KMnO_4$. The acids were extracted with ether by continuous extraction. Ether was distilled off (fractionating column), the residue (8 g) distilled under vacuum (water-pump). Four fractions were obtained: 1st 33-45° (68 mm), 2nd 45-80° (68-52 mm), 3rd 80-115° (52-30 mm), 4th 115-132° (30-29 mm).

In the 1st and 2nd fractions acetic acid was found after second fractional distillation, in the 3rd propionic acid and valeric acid, and in the 4th caproic acid (unlike valeric acid, caproic acid gave a white crystalline precipitate with zinc acetate). Ozonolysis results indicate that the olefins obtained on hydrogenation of vinylbutylacetylene are a mixture of octene-1, octene-2 and octene-3.

There are data in the literature concerning various octenes [4] and 1,2-dibromooctane [9]; there is no information about 2,3- and 3,4-dibromooctanes.

Comparison of our data and literature data confirms the conclusions made by us on the basis of ozonolysis results.

25.3 g tetrabromide treated with zinc in aqueous alcohol solution yielded 3.2 g hydrocarbon. Distillation of the latter at normal pressure at 130-131° gave 2.1 g of a product with n_D^{20} 1.4499, d_4^{20} 0.7578; residue 1 g.

There are no data in the literature with respect to octadiene-1,3 and 1,2,3,4-tetrabromooctane. On the basis of considerations mentioned above in connection with heptadiene and tetrabromoheptane it may be concluded that the diolefin obtained by us on hydrogenation of vinylbutylacetylene was octadiene-1,3 and the bromide correspondingly 1,2,3,4-tetrabromooctane.

The effect of the decelerator on the composition of hydrogenation products of vinylbutylacetylene with a molar ratio of hydrocarbon and hydrogen can be seen from the following experiments: 30.6 g vinylbutylacetylene was hydrogenated in the presence of 10 ml colloidal Pd (10 mg Pd), 250 ml methanol, 2 ml alcoholic solution p-thiocyanochlorobenzene (4 mg) at 21° and 755 mm. The calculated amount of hydrogen (2H) — 6880 ml — was taken up in 234 minutes (Table 2).

TABLE 2

Time (min.)	25	50	75	100	125	150	175	200	210	220	224	228	232	234
Vol. H (ml)	260	423	544	649	762	892	1061	1364	1825	3170	3850	5565	6280	6880
% H_2	3.8	6.1	7.9	9.5	11.0	12.9	15.4	19.8	26.6	46.0	56	80.7	91	100

The reaction mixture yielded 23.5 g hydrocarbon, fractional distillation of which gave 17.4 g product with b. p. 126-129°, n_D^{20} 1.4348, d_4^{20} 0.7431. Residue consisted of 4 g substance with n_D^{20} 1.4578, d_4^{20} 0.7829 (somewhat impure original hydrocarbon).

In another experiment, 17.92 g vinylbutylacetylene, in the presence of 5 mg Pd and 3 mg p-thiocyanochlorobenzene, gave after hydrogenation 9.55 g hydrocarbon with b. p. 126-129°, n_D^{20} 1.4347, d_4^{20} 0.7433 and a residue (3.4 g) with n_D^{20} 1.4548, d_4^{20} 0.7776 (original hydrocarbon).

Both samples of hydrocarbons combined (26 g) were treated with 24 ml bromine in 240 ml chloroform. After distilling off the solvent and repeated fractional vacuum distillations the following were obtained: 20.0 g dibromide with b. p. 92° (6 mm), n_D^{20} 1.4989, d_4^{20} 1.4585 and 41.2 g tetrabromide with b. p. 157-161° (6 mm), n_D^{20} 1,5722, d_4^{20} 1.9766.

The amount of bromides shows that the ratio of olefins to diolefins is 1:1.3.

Twenty g dibromide, treated with zinc in aqueous alcohol solution, yielded 6 g crude olefin which, on distillation gave 4 g of product with b. p. 122-123°, n_D^{20} 1.4139, d_4^{20} 0.7249; residue 1.5 g.

41.0 g tetrabromide, similarly treated, gave 7.7 g hydrocarbon which on distillation gave 4.1 g hydrocarbon with b. p. 130-131°, n_D^{20} 1.4500, d_4^{20} 0.7566, residue 2 g.

Addition of p-thiocyanochlorobenzene thus did not alter the composition of the reaction products obtained on hydrogenation of vinylbutylacetylene but retarded markedly (Table 2) the process of hydrogenation itself and changed the ratio of olefins to diolefins, increasing the yield of the latter.

SUMMARY

1. It was shown that in hydrogenation of vinylpropyl- and vinylbutylacetylene in the presence of colloidal palladium, the addition of hydrogen occurs at the triple bond as in the case of vinylmethyl- and vinylethylacetylene, with simultaneous further hydrogenation of the 1,3-dienes formed to the corresponding ethylene hydrocarbons.

2. It was established that the addition of a small amount of p-thiocyanochlorobenzene enhanced the selectivity of hydrogenation.

3. Octadiene-1,3, 1,2,3,4-tetrabromoheptane and tetrabromooctane were characterized for the first time; more precise constants are given for heptadiene-1,3.

LITERATURE CITED

[1] Kh. V. Bal'ian, A. A. Petrov and Iu. I. Porfirieva, J. Gen. Chem. 26, 1926 (1956).*

[2] R. A. Jacobson and W. H. Carothers, J. Am. Chem. Soc. 55, 1622 (1933).

[3] Kh. V. Bal'ian, J. Gen. Chem. 21, 721 (1951).*

[4] K. N. Campbell and L. T. Eby, J. Am. Chem. Soc. 68, 2683 (1911); Soday Boord, J. Am. Chem. Soc. 55, 3293 (1933); M. Tuot, Compt. rend. 211, 561 (1940).

[5] Dictionary of Organic Compounds,** I, 695 (1949).

[6] K. I. Karasaev, J. Gen. Chem. 10, 1699 (1940).

[7] Dictionary of Organic Compounds** II, 149 (1949).

[8] Dictionary of Organic Compounds** Vol. 2, p. 47.

[9] Dictionary of Organic Compounds** Vol. 1, p. 711.

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**Russian translation.

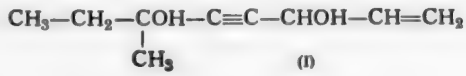
SYNTHESIS OF 6-METHYLOCTENE-1-YNE-4-DIOL-3,6 AND 7-METHYLOCTENE-2-YNE-5-DIOL-4,7 AND THEIR CATALYTIC HYDROGENATION

A. I. Nogaideli, K. Ia. Dzagnidze and R. Papava

We established in a previous communication [1] that the magnesium bromo derivative of dimethylacetylenylcarbinol reacted normally with acrolein at -7° to form ene-yne glycol— 6-methylheptene-1-in-4-diol-3,6. This ene-yne glycol, in the presence of colloidal palladium, adds on energetically 4 atoms of hydrogen, the last 2 atoms of hydrogen being added on more slowly [1].

It seemed interesting to synthetize other homologs of this class and to study the character of hydrogenation in the presence of catalysts.

6-Methyloctene-1-yne-4-diol-3,6 (I) was synthetized by the Zh. I. Iotsich method from methylethylacetylenylcarbinol and acrolein.

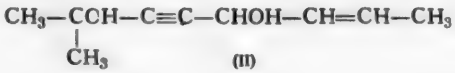


(I)

Study of the hydrogenation reaction showed that in the presence of platinum black the rate of reaction of hydrogenation gradually decreased and there was no discontinuity after the addition of two or four atoms of hydrogen, although the first 2 atoms of hydrogen added on more slowly. In the presence of colloidal palladium, however, the eninglycol behaved like the first homolog [1], i.e., it added on the first 4 atoms of hydrogen more energetically with a sharp break and much slower addition of the last 2 atoms of hydrogen.

The product of exhaustive hydrogenation (over Pt and Pd) is a mobile oil. Analysis confirms that this substance is a saturated glycol 3-methyloctandiol-3,6.

Crotonaldehyde and dimethylacethylenylcarbinol gave a second eninglycol 7-methyloctene-2-yne-5-diol-4,7 (II).



(II)

Hydrogenation of this substance in the in the presence of colloidal palladium showed a sharp change in the rate of reaction soon after the addition of two atoms of hydrogen. Hydrogenation proceeds even more slowly when platinum black is used.

Treatment of the hydrogenation product yields a colorless fairly thick oil, analysis of which confirms that it is the saturated glycol 2-methyloctandiol-2,5.

EXPERIMENTAL

Synthesis of 6-methylocten-1-yne-4-diol-3,6. The glycol was prepared in the usual way from 12 g magnesium, 56 g ethyl bromide, 21 g methylethylacetylenylcarbinol and 25 g acrolein. Yield 60.67%.

b. p. 144-145° (20 mm), d_{17}^{17} 0.9947, n_D^{17} 1.4850, MR_D 44.37; calc. 44.34.

Found %: C 70.04; H 8.92; OH 21.10. $C_9H_{12}(OH)_2$. Calculated %: C 70.10; H 9.00; OH 22.07.

Synthesis of 7-methylocten-2-yne-5-diol-4,7. The glycol was obtained from 12 g magnesium, 56 g ethyl bromide, 21 g dimethylacetylenylcarbinol and 35 g freshly distilled crotonaldehyde. The main reaction product distilled over at 100-108° (4 mm). Yield 18.5 g (26%).

d_{20}^{20} 1.0280, n_D^{20} 1.5210, MR_D 45.90; calc. 44.29.

Found %: C 69.48; H 10.9; OH 22.07. M 153.1 (cryoscopy) $C_9H_{12}(OH)_2$. Calculated %: C 70.12; H 9.9; OH 23.99. M 154.

Hydrogenation of 6-methylocten-1-yne-4-diol-3,6. Catalytic hydrogenation of the glycol was carried out in 50 ml ethyl alcohol. Results of hydrogenation are given in Table 1.

Saturated glycol 3-methyloctandiol-3,6 distilled over at 119-122° (4 mm).

d_{20}^{20} 0.9742, n_D^{20} 1.4643, MR_D 46.53; calc. 46.81.

Found %: C 67.80; H 12.50; OH 21.00. M 165 (cryoscopy) $C_9H_{18}(OH)_2$. Calculated %: C 67.50; H 12.59; OH 21.25. M 160.

TABLE 1

Expt. No.	Name of glycol*	Catalyst	Catalyst sample (mg)	Amount hydrogen (ml)		
				calc.	found	Uptake every 6 min.
1	6-Methylocten-1-yne-4-diol-3,6	Pt black	750	760	763	290. 190. 154. 105. 70. 15. 5. 2. 2. 1.
2	The same	Colloidal Pd	3	760	762	385. 209. 76. 42. 19 etc.; a total of 762 ml added on in 48 min.

*Sample of glycol in both experiments was 1.54 g.

TABLE 2

Expt. No.	Name of glycol	Sample of glycol (g)	Catalyst	Amount catalyst (mg)	Amount of hydrogen (ml)		
					calc.	found	Uptake every 6 min.
1	Methylocten-2-yne-diol-4,7	1.547	Colloidal Pd	50	761	765.	178, 118, 56, 40 etc.; a total of 765 ml added on in 240 min.
2	The same	1.516	Pt black	750	754	755	Hydrogenation proceeded very slowly and 20 hrs. were required for the absorption of 755 ml hydrogen.

Hydrogenation of 7-methylocten-2-yne-3-diol-4,7. Catalytic hydrogenation of the glycol was carried out in 50 ml ethyl alcohol. Results of hydrogenation are given in Table 2.

After treatment of the hydrogenation product the main fraction – 2-methyloctandiol-2,5 distilled over at 116-120° (4 mm).

d_{20}^{20} 0.9645, n_D^{20} 1.4668, MR_D 46.04; calc. 46.81.

Found %: C 67.25; H 12.10; OH 19.50. M 158.2 (cryoscopy). $C_9H_{18}(OH)_2$. Calculated %: C 67.50; H 12.50; OH 21.25. M 160.

SUMMARY

1. Two enin glycols were obtained: 6-methylocten-1-yne-4-diol-3,6 (I) and 7-methylocten-2-yne-5-diol-4,7 (II), which have not been described in the literature.

2. It was shown that the first glycol, in the presence of colloidal palladium, added on energetically 4 atoms of hydrogen with a subsequent change in the rate of reaction of hydrogenation.

3. In the presence of platinum black the rate of hydrogenation of both glycols gradually slowed down with no abrupt change in the rate of reaction after addition of 2 and 4 atoms of hydrogen.

4. The second glycol underwent hydrogenation much more slowly than the homologs described by us previously, and unlike the latter added on fairly energetically only 2 atoms of hydrogen.

In the course of this work, saturated glycols 2-methyloctandiol-2,5 and 3-methyloctandiol-3,6 were isolated and characterized.

LITERATURE CITED

[1] A. I. Nogaideli, K. Ia. Dzagnidze and N. Uridiia, J. Gen. Chem. 25, 2225 (1955).*

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*Original Russian pagination. See C. B. Translation.

INVESTIGATION OF LIGNIN IN HUSKS OF COTTON SEEDS

A. F. Semechkina and N. N. Shorygina

The composition of the cotton seed husks has been studied by a number of workers [1-7]. These works show that the composition of the husk depends on the sort of cotton, degree of its ripeness, amount of lint on the seeds etc. The amount of separate components in the husk fluctuates considerably [6]: ash 2-2.85, pentosans 21.6-27.6, cellulose 36-48.5, lignin 19.6-32, oils and resins 2.1-3.8, uronic acids 4.4-5.5, proteins 3-9%. The methoxyl group content of the husks is 0.98-1.87%.

The data cited show that despite the considerable lignin content of the husks, the amount of methoxyl groups is one-third to one-quarter of that found in the wood of conifers, and in deciduous wood it is 3.5-4.5 times higher than in the husks. This indicates either that the lignin in cotton seed husks is very different in its composition from wood lignins or that its content in the husks is much lower than in wood. In the latter case the isolated lignin is contaminated by products of carbohydrate humification.

In order to elucidate these questions an investigation of the cotton seed husk lignin was undertaken. Lignin was isolated from the husks by various means. Comparison was made of the yields and analyses of the lignins obtained. In addition, oxidation of husks with nitrobenzene and alkali was carried out.

Husks from ripe cotton seeds from the Ferganskii Hydrolysis Plant were used for obtaining lignin.

The husks were covered with lint and had the following composition: ash 2.31%, resinous substances 1.42%, lignin according to Koenig 33.35%, OCH_3 1.50%, pentosans 25.29%, lint ~20%.

Lignin from husks twice extracted with dichloroethane was isolated: 1) according to the copper-ammonia method of Freudenberg [8] modified to the extent that, owing to the marked viscosity of the cellulose solution on initial treatment, the amount of copper-ammonia solution was increased to 4 liters per 100 g husks; 2) by the hydrochloric acid method lignin was isolated from the husks both after treatment with 5% NaOH and without alkaline treatment; 3) by precipitation of lignin with acid from alkaline solution obtained by treating dichloroethane-extracted husks with 5% solution of NaOH and separation of lignin from hemicelluloses by treatment of the precipitate (obtained by acidifying the solution) with alcohol.

The yields and composition of the lignins are presented in the table which shows that lignins isolated by the classic methods from cotton husks are markedly different from wood lignins obtained by the same methods. The methoxyl group content of these lignins is considerably lower than of wood lignins.

In order	Method of isolation	Yield, dry husks (%)	OCH_3 in lignin (%)	Content in lignin (%)	
				C	H
1	Copper-ammonia method	8	3.99	57.14	5.07
2	Hydrochloric acid method	17	4.28	59.04	4.62
3	Lignin isolated by the Koenig method	33.35	3.66		
4	Alkaline lignin	1	9.64	56.13	5.65

By oxidizing cotton husks with nitrobenzene and alkali a mixture of aldehydes was obtained. Their yield from dichloroethane-extracted husks was 1.58% (1.98% with reference to husks without lint and 4.73% with reference to Koenig lignin). The methoxyl group content of the aldehydes was 26.4% and crystals of vanillin were deposited after a period of standing.

Paper chromatography revealed the presence of vanillin and syringic aldehyde. The methoxyl group content of the aldehydes indicates that syringic aldehyde and vanillin are present in the mixture in the ratio 1.1 : 1.4. No n-hydroxybenzaldehyde was found in the aldehyde mixture.

The aldehyde composition shows that the "natural lignin of cotton seed husks is close to lignin of deciduous wood. However, husks yield much less lignin than the wood of deciduous plants. Investigation of cotton seed husk lignin is continuing.

EXPERIMENTAL

Isolation of lignin by the copper-ammoniacal method. Cotton seed husks were extracted twice with dichloroethane. The extracted husks were treated twice with a 5% aqueous solution of sodium hydroxide over a period of 24 hours at room temperature, with shaking; they were then washed with water, dilute acetic acid and again with water. Air-dried husks (without preliminary boiling with 1% H_2SO_4) were shaken for 12 hours with copper-ammoniacal solution in a flask filled to the top with the solution.

4000 ml solution (containing 1.3 g copper per 100 ml) was used for 100 g husks. The undissolved part of the husks was filtered off, washed with ammonia, water, dilute hydrochloric acid and again with water. The residue was boiled with 1% sulfuric acid and after drying again shaken with copper-ammoniacal solution (750 ml per 100 g). Boiling with 1% solution of sulfuric acid and treatment with copper-ammoniacal solution were repeated once again. The lignin obtained was in the form of a dark powder; yield 8%.

Alkaline lignin. The dark reddish-brown solution obtained by treating the husks with 5% solution of sodium hydroxide (after extraction with dichloroethane) was acidified to Congo, when a gelatinous precipitate came down. The precipitate was filtered off, washed with water and then treated with ethyl alcohol at room temperature. The alcohol was removed from the extract and a fine pale-brown powder was obtained in the residue. Its yield was 1% of the husk weight.

Oxidation of the husks with nitrobenzene and alkali. The extracted husks (100 g) were mixed with 2 N solution of sodium hydroxide (1200 g) and nitrobenzene (100 g). The mixture was heated at 160° for 3 hours in an autoclave, with stirring. The contents of the autoclave were then transferred to a flask from which the nitrogen-containing substances were removed by steam-distillation. After cooling, the contents of the flask were filtered and the clear filtrate neutralized with sulfuric acid. 20 ml concentrated sulfuric acid was then added and the pH of the solution brought to 7.3 by the addition of Na_3PO_4. The mixture was extracted with trichloroethylene. The extract was shaken with 5% solution of sodium bisulfite. The bisulfite solution was acidified with sulfuric acid and the SO_2 driven off by gentle heating of the mixture on a water bath and passing CO_2 through it. After this the solution was extracted with ether. The ethereal extract was dried and the ether distilled off. In the residue was a product which was in the form of pale-yellow oil which tended to thicken and had a strong odor of vanillin. Fine needles of crystalline vanillin appeared on the surface, after a period of standing. Yield of aldehydes 1.58 g.

Paper chromatographic investigation of the aldehyde mixture. "Crab paper" (parchment-like base) prepared at the Leningrad Volodarskii Paper Mill No. 2 was used for this investigation. The developing solvent for the aldehydes was the mixture: ligroin + n-butyl alcohol + water in the ratio 6 : 1 : 1. The position of the aldehydes on the paper was found with the help of 0.2% solution of 2,4-dinitrophenylhydrazine in 2 N HCl.

SUMMARY

1. The husks of cotton seeds contain considerably less methoxyl groups than wood; this also applies to lignin isolated from cotton husks as compared with isolated wood lignins.

This means that the content of aromatic elements common for wood lignins is lower in cotton seed husks than in wood.

2. The composition of cotton seed husk lignin includes elements which contain the aromatic nuclei of syringic and guaiacyl structure.

No elements with hydroxyphenyl radicals were found in this lignin.

LITERATURE CITED

[1] N. M. Chetverikov, Butter and Fat Industry, No. 2, 34 (1932).

[2] N. M. Chetverikov and A. I. Lazarev, Chemical Treatment of Agricultural Waste Products,* Food Industry Press (1935).

[3] P. N. Odintsov, M. N. Tsipkina and L. V. Egorova, J. Ind. Chem. 9, 119 (1936).

[4] V. I. Sharkov, Hydrolysis Industry, vol. I, 34 (1945).

[5] B. L. Matkul, Works of the Uzbek. Philological Acad. Sci. USSR, Ser. VII, No. 3, 22 (1941).

[6] I. M. Orlova, Hydrolysis Industry, No. 1 (1950).

[7] A. P. Zakoshchikov, Hydrolysis Industry, No. 1 (1951).

[8] Freudenberg, Harder and Market, Ber. 61, 1762 (1928).

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*In Russian.

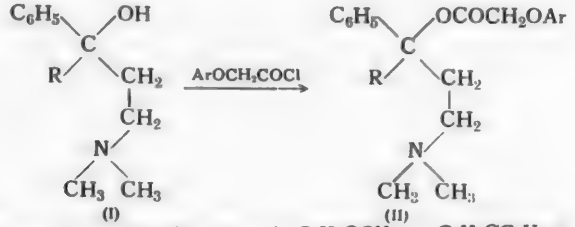
SYNTHETIC ANESTHETICS

XXII. PHENOXYACETATES OF 1-PHENYL-3-DIMETHYLAMINOPROPAN-1-OLS

I. N. Nazarov and E. M. Cherkasova

Previous papers [1,2] describe the preparation of a series of esters of 1-phenyl-3-dialkylaminopropan-1-ols and among them were found some compounds with a high anesthetic activity. Thus, for example, the phenoxyacetate of 1-phenyl-1-ethyl-3-dimethylaminopropan-1-ol was found to be a very strong anesthetic, as active as dicaine but considerably less toxic. In connection with this, it seemed interesting to synthesize a series of other phenoxyacetates of 1-phenyl-3-dialkylaminopropan-1-ols and to follow systematically the relation between the structure of these compounds and their physiological activity.

For this purpose we prepared some substituted phenoxyacetates of 1-phenyl-3-dimethylaminopropan-1-ol, containing various substituents in the benzene nucleus of the phenoxyacetate group.

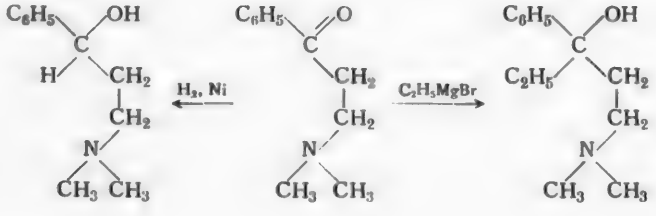


(I) (II)

R = H, C_2H_5; Ar = $C_6H_4CH_3$ (o-,m-,p-), $C_6H_4OCH_3$-p, $C_6H_4OC_2H_5$-p, $C_6H_3Cl_2$ (2,4)

In order to test the anesthetic effect, we also prepared the cinnamic ester of the amino alcohol (I, R=H) as in some other cases such esters were found to be valuable [1].* We attempted to reduce the p-nitrobenzoate of the amino alcohol (I, R = C_2H_5) with stannous chloride and hydrochloric acid to the corresponding p-aminobenzoate, but this reaction gave a very small yield. Attempts at catalytic reduction gave negative results.

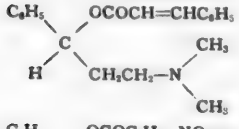
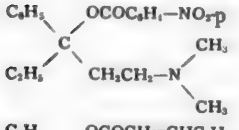
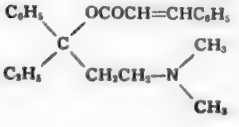
The starting amino alcohols (I) were prepared, as described previously [1], by the Mannich reaction from acetophenone and dimethylamine followed by reduction of the β-dimethylaminopropiophenone thus formed or treatment of it with a Grignard reagent:



*See table of anesthetic activity.

The esters (II) obtained were tested pharmacologically as the hydrochlorides in the laboratory of M. D. Mashkovskii and it was found that the cinnamic ester of 1-phenyl-3-dimethylaminopropan-1-ol and the p-nitrobenzoate and m-cresoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol were active surface anesthetics. The p-cresoxyacetate and p-methoxyphenoxyacetate of the tertiary alcohol (I, R = C_2H_5) had activities approaching that of dicaine as their indexes in a 0.5% solution were 1200 and 1180 respectively (1300 for dicaine) but the activities of the solutions dropped sharply after sterilization. Thus, the introduction of a methyl or methoxyl group into the position para to the phenolic hydroxyl decreased the stability of the phenoxyacetates described, to hydrolysis. As could be expected, the 2,4-dichlorophenoxyacetate of the amino alcohol (I, R = C_2H_5) had a strong irritating effect; a 0.5% solution of it caused strong edema of the mucous membrane of a rabbit's eye and therefore, was not investigated in detail. The o-cresoxyacetate of the amino alcohol (I, R = C_2H_5) was not investigated for the same reason, while the p-ethoxyphenoxyacetate was insoluble in water. The results of the tests are summarized in the table.

The Anesthetic Activity of The Hydrochlorides of Phenoxyacetates (II) and Others

Formula of preparation	Index	
	anesthesia (0.5%)	after sterilization (0.5%)
Dicaine	1300*	1300
(II) R = C_2H_5, Ar = $C_6H_4CH_3$-p	1200	56.5
(II) R = C_2H_5, Ar = $C_6H_4OCH_3$-p	1180	22.5
(II) R = C_2H_5, Ar = $C_6H_3Cl_2$(2, 4)	Has irritating effect	
(II) R = C_2H_5, Ar = $C_6H_4CH_3$-o	Has irritating effect	
(II) R = C_2H_5, Ar = $C_6H_4OC_6H_5$-p	Soluble in water only on heating	
(II) R = C_2H_5, Ar = $C_6H_4CH_3$-m	951	
	354	
	413	
	1067** (0.25%)	Activity remained unchanged

*Average fatal dose 8 mg/kg.

**Average fatal dose 35 mg/kg.

EXPERIMENTAL

The acid chlorides of the substituted phenoxyacetic acids were prepared in 80-90% yields by the action of thionyl chloride on the substituted phenoxyacetic acids, which were prepared in their turn from appropriate phenols and chloroacetic acid in the presence of alkali. As an example, the preparation of o-cresoxyacetyl chloride is described below.

10 g of freshly distilled thionyl chloride (b. p. 76-78°) was added with cooling to 5 g of o-cresoxyacetic acid (m. p. 150°) [3]. The next day the mixture was heated for 4 hours on a water bath at 60-80°, the excess thionyl chloride distilled off and the residue vacuum distilled. We obtained 4 g of o-cresoxyacetyl chloride with b. p. 108-110° (6 mm) [4].

1-Phenyl-3-dimethylaminopropan-1-ol (I, R = H). 6.3 g of β-dimethylaminopropiophenone hydrochloride [5] (m. p. 152-153°) in 60 ml of anhydrous alcohol was hydrogenated in the presence of 1 g of nickel catalyst. The hydrogenation lasted for 2.5 hours and 1090 ml of hydrogen was absorbed (against 724 ml, calculated theoretically). The catalyst was filtered off, the alcohol distilled off under reduced pressure and the residue twice recrystallized from acetone. We obtained 2.34 g of 1-phenyl-3-dimethylaminopropan-1-ol hydrochloride (I, R = H) with m. p. 132-133° [5].

Found %: N 6.53, 6.68. $C_{11}H_{17}ON \cdot HCl$. Calculated %: N 6.5.

Cinnamate of 1-phenyl-3-dimethylaminopropan-1-ol. 6.5 g of cinnamyl chloride (m. p. 35°) in 8 ml of benzene was added to a solution of 1.5 g of 1-phenyl-3-dimethylaminopropan-1-ol in 5 ml of anhydrous benzene. The mixture, which rapidly crystallized, was heated for 2 hours at the boiling point of the benzene. The next day the precipitated crystals were washed with absolute ether and treated with 25% ammonia. The liberated base was extracted with ether and dried with sodium sulfate. After distilling off the ether and the starting amino alcohol (b. p. 107° at 2 mm, hydrochloride, m. p. 130-132°, 0.6 g), we directly converted the residue into the hydrochloride in a chloroform solution. We obtained 1.05 g of the cinnamate of 1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 176-176.5°.

Found %: C 69.71, 69.60; H 6.82, 6.92; N 4.08, 3.95. $C_{20}H_{23}O_2N \cdot HCl$. Calculated %: C 69.45; H 6.94; N 4.05.

From the benzene mother liquors we isolated 0.9 g of the hydrochloride of the starting amino alcohol with m. p. 132-133°.

o-Cresoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol (II, R = C_2H_5, Ar = $C_6H_4CH_3$-o). To a solution of 1.2 g of freshly distilled 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol [1] in 5 ml of anhydrous benzene was added 0.1 g of magnesium and then 2.5 g of freshly distilled o-cresoxyacetyl chloride (b. p. 106-107° at 6 mm) in 5 ml of anhydrous benzene gradually was added with cooling in ice water. The mixture was kept for 2 days at room temperature and then the precipitate was filtered off, washed with ether and recrystallized from anhydrous acetone with the addition of a small amount of ether until the acetone solution became turbid. We obtained 1.7 g of the o-cresoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 146-148°.

Found %: C 67.02, 66.50; H 7.96, 7.96; N 3.37, 3.61. $C_{22}H_{29}O_3N \cdot HCl$. Calculated %: C 67.50; H 7.70; N 3.56.

m-Cresoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol (II, R = C_2H_5, Ar = $C_6H_4CH_3$-m). To 2 g of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol [1], cooled in ice, was added 4 g of m-cresoxyacetyl chloride (b. p. 89-91° at 3 mm) [4]. The mixture was heated for 3 hours on a boiling water bath, after which anhydrous ether was added with cooling. The following day the precipitate obtained was filtered off, washed with ether and recrystallized 5 times from acetone. We obtained 0.62 g of the m-cresoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 156-157°.

Found %: C 66.62; 66.82; H 7.75, 7.71; N 3.64, 3.68. $C_{22}H_{29}O_3N \cdot HCl$. Calculated %: C 67.50; H 7.70; N 3.56.

p-Cresoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol (II, R = C_2H_5, Ar = $C_6H_4CH_3$-p). 2 g of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol [1], 0.2 g of magnesium turnings, 5 g of p-cresoxyacetyl chloride (b. p. 85-88° at 3 mm) and 14 ml of anhydrous ether were used. The mixture was treated as in the previous experiment. We obtained 0.8 g of the p-cresoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 145-146° (from acetone).

Found %: C 67.18, 66.85; H 7.57, 7.58; N 3.95, 3.73. $C_{22}H_{29}O_3N \cdot HCl$. Calculated %: C 67.50; H 7.70; N 3.56.

p-Methoxyphenoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol (II, R = C_2H_5, Ar = $C_6H_4OCH_3$-p). 2 g of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol [1] and 4 g of freshly distilled p-methoxyphenoxyacetyl chloride (b. p. 121-123° at 3 mm) [6] were mixed and cooled in ice water. The mixture was heated for 4 hours on a boiling water bath and kept for several days at room temperature. The glassy mass precipitated was triturated several times with anhydrous ether (50 ml). The ether was poured off and the residue twice recrystallized from acetone. We obtained 0.23 g of p-methoxyphenoxyacetate hydrochloride with m. p. 148-149°. The acetone was distilled off from the mother liquors and the residue dissolved in 15 ml of anhydrous alcohol and boiled for 15 minutes with animal charcoal. The latter was filtered off, ether added until the alcohol solution became turbid and the precipitate recrystallized from acetone. We obtained a further 2.4 g of the p-methoxyphenoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 147-148°.

Found %: N 3.63, 3.74. $C_{22}H_{29}O_4N \cdot HCl$. Calculated %: N 3.44.

p-Ethoxyphenoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol (II, R = C_2H_5, Ar = $C_6H_4OC_2H_5$-p). 1.5 g of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol [1], 3.5 g of freshly distilled p-ethoxyphenoxyacetyl chloride (b. p. 120-125° at 3 mm) and 25 ml of a mixture of anhydrous acetone, benzene and ether (1:1:1) were used. The mixture was heated on a water bath for 1.5 hours. The following day the precipitated mass was triturated with ether and the residue separated off, washed with ether and recrystallized 4 times from acetone. We obtained 0.89 g of the p-ethoxyphenoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 160-161°.

Found %: C 65.18, 65.49; H 7.87, 7.79; N 3.62, 3.52. $C_{23}H_{31}O_4N \cdot HCl$. Calculated %: C 65.48; H 7.53; N 3.32.

2,4-Dichlorophenoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol [II, R = C_2H_5, Ar = $C_6H_3Cl_2$ (2,4)]. 5.8 g of 2,4-dichlorophenoxyacetyl chloride (m. p. 45°) [7] in 10 ml of benzene was added to a solution of 2 g of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol in 5 ml of benzene, cooled in ice water. The mixture was heated for 4 hours at 80-85°. The following day the reaction mass was treated as described in the previous experiment. We obtained 1.93 g of the 2,4-dichlorophenoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 159-160° (from acetone).

Found %: C 56.75, 56.65; H 6.18, 6.03; N 3.14, 3.23. $C_{21}H_{25}O_3NCl_2 \cdot HCl$. Calculated %: C 56.4; H 5.8; N 3.17.

p-Nitrobenzoate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol. 4 g of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol [1], 10.9 g of p-nitrobenzoyl chloride (m. p. 73°) [8] and 10 ml of chloroform were heated on a water bath at 70-75° for 2 hours. The following day the reaction mass was treated as described above. We obtained 3.6 g of the p-nitrobenzoate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 157-158° (from anhydrous alcohol).

Found %: C 60.92; 60.88; H 6.73, 6.63; N 7.26, 7.27. $C_{20}H_{24}O_4N_2 \cdot HCl$. Calculated %: C 61.10; H 6.36; N 7.10.

SUMMARY

A series of substituted phenoxyacetates of 1-phenyl-3-dimethylaminopropan-1-ols, which are active local anesthetics, were synthesized. However, none of these esters were more interesting as anesthetics than the unsubstituted phenoxyacetates.

LITERATURE CITED

[1] I. N. Nazarov and E. M. Cherkasova, J. Gen. Chem. 25, 1536 (1955).*

[2] I. N. Nazarov and E. M. Cherkasova, J. Gen. Chem. 25, 1935 (1955).*

[3] Beilst., 6, 356.

[4] Higginbotham and Stephen, J. Chem. Soc. 117, 1538 (1920).

[5] Mannich and Heilner, Ber. 55, 356 (1922).

[6] U. S. Patent 2478366 (1949); Ch. A. 6313 (1950).

[7] Freed, J. Am. Chem. Soc. 68, 2112 (1946).

[8] Synth. Org. Prep., I, 472 (1949).

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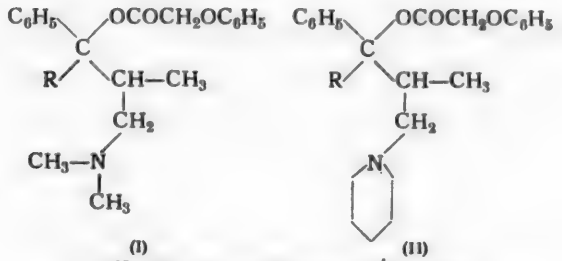
SYNTHETIC ANESTHETICS

XXIII. PHENOXYACETATES OF 1-PHENYL-2-METHYL-3-DIALKYLAMINOPROPAN-1-OLS

I. N. Nazarov, E. M. Cherkasova and Ch'ang Ch'ung Kwang

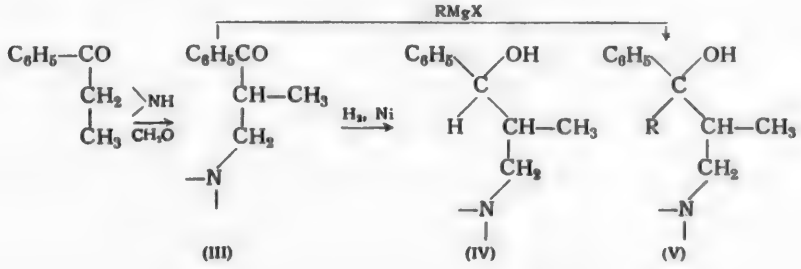
As highly active anesthetics were found among the phenoxyacetates of 1-phenyl-3-dialkylaminopropan-1-ols [1], we synthesized a series of phenoxyacetates of 1-phenyl-2-methyl-3-dialkylaminopropan-1-ols, represented by formulas (I) and (II), in order to elucidate the effect of the methyl group in the propanol chain on the physiological activity of these compounds.



(I) (II)

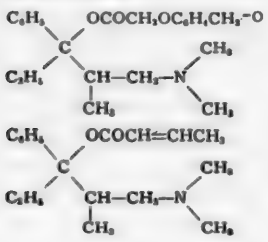
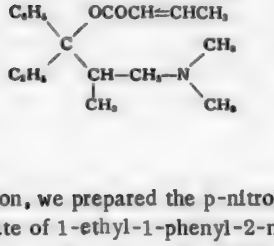
R=H, CH_3, C_2H_5, n.-C_3H_7, n.-C_4H_9, iso-C_4H_{11}.

Using other examples, the positive effect of such branching in the alkanolamine chain on the physiological (anesthetic) activity of the esters had been noted previously [2]. The starting 1-phenyl-2-methyl-3-dialkylaminopropan-1-ols were prepared, as described previously [2], from propiophenone by the Mannich reaction. The amino ketones (III) thus formed were hydrolyzed to the corresponding secondary amino alcohols (IV) or were converted into tertiary amino alcohols (V) by treatment with Grignard reagents.



(III) (IV) (V)

Dimethylamine and piperidine were used as secondary amines in the Mannich reaction. The amino alcohols (IV) and (V) obtained, were converted into the corresponding phenoxyacetates by treatment with phenoxyacetyl chloride.

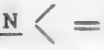
Formula of preparation	Anesthesia index				Anesthesia index after sterilization (0.25%)	Average fatal dose (in mg/kg)
	0.1%	0.25%	0.5%	1%		
Dicaine	947	1196	1300	1300		8.5
(II) R = C_2H_5	947	1300		1300	897	6.7
(II) R = CH_3	645	1146		1264	957	11
(I) R = n-C_4H_9		1300		1300	219	
		1300		1300	Precipitates	
			65			

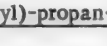
In addition, we prepared the p-nitrobenzoate of 1-ethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol, the o-cresoxyacetate of 1-ethyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol and the crotonic ester of this amino alcohol so as to compare it with the cinnamic ester of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol, whose activity was extremely high [9].

Some of the esters synthesized were tested as hydrochlorides in a pharmacological laboratory for surface anesthesia and were found to be strong anesthetics, similiar in activity to dicaine. The results of the tests are summarized in the table.

The phenoxyacetates (II, R = H, n-C_4H_9) were not tested due to their insolubility in water. The p-nitrobenzoate of 1-ethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol was not tested for the same reason.

EXPERIMENTAL

<u>β-Piperidylisobutyrophenone (III, N</u>  A mixture of 40.2 g of propiophenon (b. p. 213-214°), 36.4 g of piperidine hydrochloride, 16 g of paraformaldehyde, 1 ml of concentrated hydrochloric acid and 100 ml of ethyl alcohol was heated for 8 hours on a boiling water bath. During this time a further 20 g of paraformaldehyde was added. The solvent was distilled off under reduced pressure and the residual mass recrystallized from a mixture of acetone and alcohol (5:1). We obtained 59 g (73%) of β-piperidylisobutyrophenone hydrochloride with m. p. 168-170° [3,4].

<u>1-Phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (IV, N</u>  . 16.05 g of β-piperidylisobutyrophenone hydrochloride (m. p. 168-178°) in 100 ml of anhydrous ethyl alcohol was hydrogenated with continuous shaking in the presence of 0.82 g of palladium on calcium carbonate (5% palladium). The hydrogenation lasted for 16 hours and during this time a further 1.6 g of catalyst was added. 1400 ml of hydrogen was absorbed against 1458 ml calculated theoretically. The catalyst was filtered off, the alcohol distilled off, the residue acidified with dilute hydrochloric acid, the neutral products extracted with ether and the aqueous layer treated with a saturated solution of sodium hydroxide and extracted several times with ether. The ether solution was dried with sodium sulfate and the residue after evaporation of the ether was vacuum distilled. We obtained 11.8 g (84%) of 1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol with b. p. 134-136° (2 mm), m. p. 49-50.5°.

Found %: N 6.09, 6.07. $C_{15}H_{23}ON$. Calculated %: N 6.00.

The amino alcohol hydrochloride melted at 225-227° (from alcohol).

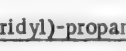
Found %: N 5.03, 4.98. $C_{15}H_{23}ON \cdot HCl$. Calculated %: N 5.19.

1,2-Dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (V, R = CH_3, N ). With continuous stirring, 26.7 of β-piperidylisobutyrophenone hydrochloride was gradually added to an ether solution of methylmagnesium iodide, prepared from 47.4 g of methyl iodide, 7.2 g of magnesium and 130 ml of absolute ether, at a temperature of -12°. The following day the reaction mixture was acidified to Congo with dilute hydrochloric acid, the ether layer separated and the aqueous acid layer saturated with alkali and extracted several times with ether. The ether extract was dried with sodium sulfate. After vacuum distillation, the product crystallized (over 10 days). We obtained 19.2 g (77.5%) of 1,2-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol with m. p. 39-40° and b. p. 133-137° (1.5 mm).

Found %: N 5.65, 5.32. $C_{16}H_{25}ON$. Calculated %: N 5.67.

The hydrochloride melted at 200-202° (from acetone).

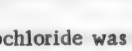
Found %: N 5.26, 4.94. $C_{16}H_{25}ON \cdot HCl$. Calculated %: N 4.94.

1-Ethyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (V, R = C_2H_5, N ) Under the conditions described above, 26.7 g of β-piperidylisobutyrophenone was added to the Grignard reagent prepared from 7.2 g of magnesium, 36.3 g of ethyl bromide and 100 ml of absolute ether. After working up the product as described in the previous experiment, we obtained 20.8 g (79.6%*) of 1-ethyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol with m. p. 64-65°.

Found %: C 78.35, 78.30; H 10.03, 10.15; N 5.01, 4.92. $C_{17}H_{27}ON$. Calculated %: C 78.20; H 10.07; N 5.30.

The hydrochloride had m. p. 210-212°.

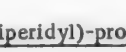
Found %: N 4.77, 4.62. $C_{17}H_{27}ON \cdot HCl$. Calculated %: N 4.72.

1-n-Propyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (V, R = n-C_3H_7, N ). 26.7 g of β-piperidylisobutyrophenone hydrochloride was added to the Grignard reagent, prepared from 7.2 g of magnesium, 41 g of n-propyl bromide and 150 ml of absolute ether. After working the product up in the usual way, we obtained 13.6 g (50%) of 1-n-propyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol with m. p. 58°.

Found %: C 78.56, 78.84; H 10.59, 10.20; N 5.16, 5.28. $C_{18}H_{29}ON$. Calculated %: C 78.5; N 10.5; H 5.1.

The hydrochloride melted at 185-186° (from acetone).

Found %: N 4.51, 4.66. $C_{18}H_{29}ON \cdot HCl$. Calculated %: N 4.50.

1-n-Butyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (V, R = n-C_4H_9, N ). 26.7 g of β-piperidylisobutyrophenone hydrochloride was added to the Grignard reagent, prepared from 7.2 g of magnesium, 47.5 g of n-butyl bromide and 100 ml of anhydrous ether. After working up the product in the

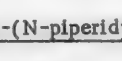
*This alcohol was prepared [5] in 26.5% yield and the hydrochloride had m. p. 216-218°.

usual way, we obtained 20.7 g (71.5%) of 1-n-butyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol with m. p. 41-42°.

Found %: N 4.89, 4.70. $C_{19}H_{31}ON$. Calculated %: N 4.84.

The hydrochloride melted at 155-156° (from acetone).

Found %: N 4.36, 4.18. $C_{19}H_{31}ON \cdot HCl$. Calculated %: N 4.30.

1-Isoamyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (V, R = iso-C_5H_{11}, N ).

A Grignard reagent was prepared from 7.2 g of magnesium, 51 g of isoamyl bromide and 100 ml of absolute ether. In the usual way, 26.7 g of β-piperidylisobutyrophenone hydrochloride was added to it. The mixture was worked up as described above. We obtained 24.75 g (81.5%) of 1-isoamyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol with b. p. 158-162° (2 mm).

Found %: N 4.49, 4.48. $C_{20}H_{33}ON$. Calculated %: N 4.62.

The hydrochloride melted at 170° (from acetone).

Found %: N 4.21, 3.97. $C_{20}H_{33}ON \cdot HCl$. Calculated %: N 4.12.

The phenoxyacetate of 1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (II, R = H). 5.25 g of phenoxyacetyl chloride (b. p. 102-104° at 9 mm) [6] was added dropwise, followed by 5 drops of sulfuric acid, to 46.6 g of 1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol in 30 ml of anhydrous ether at 0°. The mixture was left for 2 days and then heated for 1 hour at the boiling point of the ether. The precipitate was separated, washed with ether and triturated in the hot with anhydrous acetone. The insoluble residue was filtered off (2.68 g) and found to be the hydrochloride of the starting amino alcohol (m. p. 223°), which did not depress the melting point of an authentic sample.

Found %: N 5.19, 4.84. $C_{15}H_{23}ON \cdot HCl$. Calculated %: N 5.19.

A small amount of anhydrous ether was added to the acetone mother liquor and the precipitate recrystallized from acetone. We obtained 4.72 g (58.5%) of the phenoxyacetate of 1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol hydrochloride with m. p. 136-138°.

Found %: C 68.03, 67.90; H 7.31, 7.43; N 3.67, 3.73. $C_{23}H_{29}O_3N \cdot HCl$. Calculated %: C 68.3; H 7.43; N 3.47.

The phenoxyacetate of 1,2-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (II, R = CH_3). The reaction mixture consisted of 4.94 g of 1,2-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol, 5.25 g of freshly distilled phenoxyacetyl chloride and 70 ml of absolute ether and was kept for 2 hours at 0° and then for 5 days at room temperature. The precipitate was filtered off, washed with ether 3 times and recrystallized from acetone 4 times. We obtained 7.06 g (84.5%) (from all the mother liquors we isolated 4.91 g of material by a second recrystallization) of the phenoxyacetate of 1,2-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol hydrochloride with m. p. 161-163°.

Found %: C 68.62, 69.01; H 7.74, 7.55; N 3.01, 3.30. $C_{24}H_{31}O_3N \cdot HCl$. Calculated %: C 69.0; H 7.66; N 3.36.

The phenoxyacetate of 1-ethyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (II, R = C_2H_5). 5.25 g of phenoxyacetyl chloride in 20 ml of ether and 3 drops of concentrated sulfuric acid were added to a solution of 5.22 g of 1-ethyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol in 50 ml of absolute ether, cooled with ice water. The mixture was kept for a week. The ether layer was poured off and the crystalline residue (8.22 g) treated twice with absolute ether at 30° and dissolved in a mixture of chloroform and acetone by heating. On cooling, the solution deposited 0.87 g of the hydrochloride of the starting amino alcohol with m. p. 211-212°.

Found %: N 4.70, 4.61. $C_{17}H_{27}ON \cdot HCl$. Calculated %: N 4.72

Anhydrous ether was added to the mother liquor until the product completely precipitated and this was recrystallized from a mixture of chloroform and acetone. We obtained 2.77 g (32%) of the phenoxyacetate of 1-ethyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol hydrochloride with m. p. 162.5-163°.

Found %: C 69.41, 69.29; H 7.67, 7.44; N 3.41, 3.28. $C_{25}H_{33}O_3N \cdot HCl$. Calculated %: C 69.60; H 7.85; N 3.24.

The phenoxyacetate of 1-n-propyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (II, n-C_3H_7). A mixture of 4.82 g of 1-n-propyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol, 4 g of phenoxyacetyl chloride, 0.1 g of magnesium and 40 ml of absolute ether was kept for 2 days. The precipitate was washed with anhydrous ether until the smell of the acid chloride disappeared and then recrystallized from a mixture of chloroform and ether. We obtained 4.49 g (57%) of the phenoxyacetate of 1-n-propyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol hydrochloride with m. p. 176-176.5°.

Found %: C 70.22, 69.91; H 8.91, 9.22; N 2.97, 3.22. $C_{26}H_{35}O_3N \cdot HCl$. Calculated %: C 70.03; H 8.08; N 3.14.

The phenoxyacetate of 1-n-butyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (II, R = n-C_4H_9). A mixture of 5.78 g of 1-n-butyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol, 5 g of phenoxyacetyl chloride and 70 ml of ether was treated as described in the previous experiments, after standing for 2 days at room temperature. We obtained (after 3 recrystallizations from acetone) 4.35 g (47.5%) of the phenoxyacetate of 1-n-butyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol hydrochloride with m. p. 163-165°.

Found %: C 70.59, 70.41; H 7.83, 8.02; N 3.15, 2.98. $C_{27}H_{37}O_3N \cdot HCl$. Calculated %: C 70.5; H 8.25; N 3.05.

The phenoxyacetate of 1-isoamyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (II, R = iso-C_5H_{11}). 6.06 g of 1-isoamyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol, 5 g of phenoxyacetyl chloride and 70 ml of ether were used. After standing for 3 days at room temperature, the reaction product was treated as described above. Three recrystallization from acetone yielded 5.25 g (54%) of the phenoxyacetate of 1-isoamyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol hydrochloride with m. p. 140-140.5°.

Found %: C 71.01, 71.32; H 8.15, 7.94; N 3.15, 3.28. $C_{28}H_{39}O_3N \cdot HCl$. Calculated %: C 71.0; H 8.45; N 2.96.

The p-nitrobenzoate of 1-ethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol. 3 g of 1-ethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol [5], 7.5 g of p-nitrobenzoyl chloride and 20 ml of chloroform were heated at 50-60° for 3 hours. The precipitate was triturated with anhydrous ether and purified by 3 recrystallizations from alcohol. We obtained 3.2 g (60.5%) of the p-nitrobenzoate of 1-ethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol hydrochloride with m. p. 169-170°.

Found %: C 63.86, 63.79; H 6.66, 6.88; N 6.27, 6.39. $C_{23}H_{28}O_4N_2 \cdot HCl$. Calculated %: C 63.81; H 6.75; N 6.42.

The phenoxyacetate of 1-phenyl-2-methyl-3-dimethylaminopropan-1-ol (I, R = H). 3.4 g of freshly distilled phenoxyacetyl chloride (b. p. 109-110° at 13 mm) in 4 ml of benzene was added to a solution of 1.9 g of 1-phenyl-2-methyl-3-dimethylaminopropan-1-ol [2] (m. p. 87-89°) in 6 ml of anhydrous benzene, cooled in ice water. After 3 days, anhydrous ether was added and the mixture heated on a water bath for 0.5 hours. The precipitate was separated, washed 3 times with ether and purified by recrystallization from acetone. We obtained 2.3 g (64.5%) of the phenoxyacetate of 1-phenyl-2-methyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 154-156°.

Found %: C 66.53, 66.32; H 7.44, 6.97; N 3.93, 4.22. $C_{20}H_{25}O_3N \cdot HCl$. Calculated %: C 66.1; H 7.15; N 3.85.

The phenoxyacetate of 1,2-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol (I, R = CH_3). A mixture of 2.1 g of 1,2-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol [2], 4.35 g of phenoxyacetyl chloride, 0.1 g of magnesium and 6 ml of benzene was kept for 24 hours and then worked up as described above. We obtained 2.5 g (65.2%) of the phenoxyacetate of 1,2-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 160-161° (from acetone).

Found %: C 66.36, 67.04; H 7.27, 7.55; N 3.38, 3.67. $C_{21}H_{27}O_3N \cdot HCl$. Calculated %: C 66.7; H 7.42; N 3.70.

The phenoxyacetate of 1-n-propyl-1-phenyl-2-methyl-3-dimethylamonopropan-1-ol (I, R = n-C_3H_7). From 2.4 g of 1-n-propyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol [2], 2.6 g of phenoxyacetyl chloride and 14 ml of a mixture of acetone and ether (7:3), using the procedure described above, we obtained 0.5 g (12.1%) of the phenoxyacetate of 1-n-propyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 153-155° (from acetone).

Found %: C 68.07, 68.46; H 7.51, 7.53; N 3.95, 3.70. $C_{23}H_{31}O_3N \cdot HCl$. Calculated %: C 68.10; H 7.90; N 3.46.

The phenoxyacetate of 1-n-butyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol (I, R = n-C_4H_9). After being treated as described above, 2.5 g of 1-n-butyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol [2], 4.65 g of phenoxyacetyl chloride, 0.1 g of magnesium and 6 ml of anhydrous benzene yielded 2.3 g (54.7%) of the phenoxyacetate of 1-n-butyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 172.5-174° (from acetone).

Found %: C 68.58, 68.13; H 8.05, 8.24; N 3.47, 3.32. $C_{24}H_{33}O_3N \cdot HCl$. Calculated %: C 68.7; H 8.11; N 3.34.

The o-cresoxyacetate of 1-ethyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol. From 2.2 g of 1-ethyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol [2], 3.35 g of o-cresoxyacetyl chloride [7], 0.1 g magnesium and 12 ml of anhydrous benzene by the usual method, we obtained 2.3 g (56%) of the o-cresoxyacetate of 1-ethyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 157-158° (from acetone).

Found %: C 67.64, 68.32; H 7.69, 7.82; N 3.33, 3.43. $C_{23}H_{31}O_3N \cdot HCl$. Calculated %: C 68.1; H 7.90; N 3.46.

The crotonate of 1-ethyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol. By the usual procedure, 3.32 g of 1-ethyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol [2], 3.3 g of crotonyl chloride (freshly distilled at 122-124°) [8] and 13 ml of anhydrous benzene yielded 1.5 g (30.6%) of the crotonate of 1-ethyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 182-183° (from acetone).

Found %: C 66.16, 66.12; H 8.30, 8.34; N 4.10, 4.45. $C_{18}H_{27}O_2N \cdot HCl$. Calculated %: C 66.4; H 8.60; N 4.30.

SUMMARY

In order to test them pharmacologically, we synthesized a series of phenoxyacetates of 1-phenyl-2-methyl-3-dialkylaminopropan-1-ols and some of the compounds had an anesthetic activity as strong as that of dicaine (phenoxyacetates of 1-ethyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol. 1,2-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol and 1-n-butyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol and the o-cresoxyacetate of 1-ethyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol).

LITERATURE CITED

[1] I. N. Nazarov and E. M. Cherkasova, J. Gen. Chem. 25, 1536 (1955).*

[2] I. N. Nazarov and E. M. Cherkasova, J. Gen. Chem. 25, 2120 (1955).*

[3] Ruddy and Buckley, J. Am. Chem. Soc. 72, 718 (1950).

[4] Kjaer and Petersen, Acta Chem. Scand. 5, 1145 (1951).

[5] Denton et al., J. Am. Chem. Soc. 71, 2051 (1949).

[6] Blaise and Picard, Ann. Chim. (8) 26, 274 (1912).

[7] Higginbotham and Stephen, J. Chem. Soc. 117, 1538 (1920).

[8] Staudinger, Ber. 49, 1991 (1916).

[9] I. N. Nazarov and E. M. Cherkasova, J. Gen. Chem. 28, 122 (1958).*

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OXIDATION OF ORGANIC COMPOUNDS

XV. VAPOR PHASE OXIDATION OF ETHYLBENZENE ON TIN VANADATE

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The catalytic vapor phase oxidation of alkylbenzenes with a secondary α-carbon atom has been little studied. There is only one paper on this problem [1] and it reports that passing a mixture of ethylbenzene vapor and air gave only benzoic acid. At 270-280° the yield was 41%. The purpose of this work was to study thoroughly the basic rules governing this reaction. The intermediate and final reaction products in the oxidation of ethylbenzene were especially carefully studied. Some of the intermediate compounds were oxidized under comparable conditions.

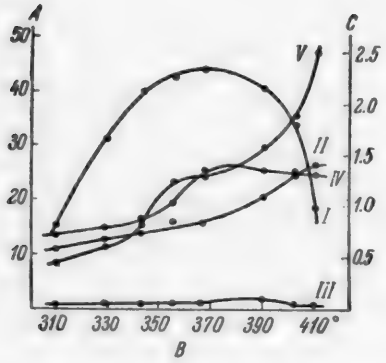
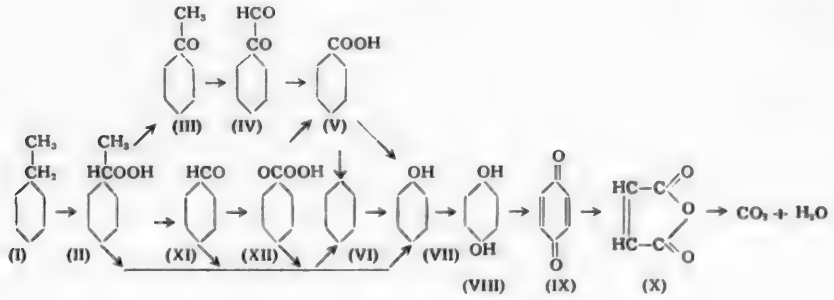


Fig. 1. Ethylbenzene oxidation. A) Yield of products of incomplete oxidation (in %), B) reaction temperature, C) CO and CO_2 yield (in moles per mole of ethylbenzene passed). I) Benzoic acid, II) maleic anhydride, III) quinone, IV) CO, V) CO_2.

The experimental data obtained showed that vapor phase oxidation of ethylbenzene with atmospheric oxygen in the presence of tin vanadate was a complex process and, depending on the conditions, formed widely differing oxygen-containing compounds. Thus, besides benzoic acid, we isolated and determined quantitatively benzaldehyde, acetophenone, quinone, maleic anhydride, CO and CO_2. The relation of the yields of some of these reaction products to temperature is shown in Fig. 1. This figure shows that there is a definite sequence in the distribution of the maxima of the yield curves of the main products of incomplete oxidation. Characteristically, the greatest amounts of quinone were formed in the temperature range at which benzoic acid yield started to decrease. A further rise in temperature was conducive to maleic anhydride formation, but then the yield of quinone and particularly that of benzoic acid fell sharply. These facts seem to indicate that in ethylbenzene oxidation, a large part of the maleic anhydride was formed from benzoic acid through the intermediate formation of quinone. This hypothesis was confirmed by the formation of quinone and maleic anhydride in the oxidation of pure benzoic acid. However, the same experiments showed that in ethylbenzene oxidation, small amounts of quinone and maleic anhydride formed also at relatively low temperatures, at which benzoic acid is stable. This indicated that two simultaneous and parallel processes for their formation were possible and these omitted the benzoic acid stage. The mechanisms for the formation of the basic products of incomplete oxidation given here were also observed in experiments with benzaldehyde, acetophenone and phenylglyoxal. In ethylbenzene oxidation, the stages of benzaldehyde and acetophenone formation, without doubt, preceded the formation of benzoic acid, but occurred parallel to each other. The only other modification possible here – the conversion of acetophenone into benzaldehyde – was not confirmed experimentally.

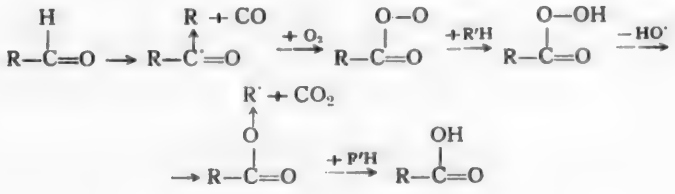
In the experiments investigated, besides the main reaction products, other oxygen-containing compounds were formed, among them phenol and peroxides. Although, only traces of these were found, their formation should also be considered as due to the existence of definite intermediate stages in the process of ethylbenzene oxidation. In connection with this, the peroxide compounds should be investigated thoroughly. We detected them only in ethylbenzene oxidation experiments carried out at a relatively low temperature.

However, the papers by K. I. Ivanov [2], V. Ia. Shtern [3] and other investigators, which prove the possibility of the formation of peroxide compounds during the oxidation of various hydrocarbons over an extremely wide temperature range, indicate that in a given case they also formed in other experiments at a higher reaction temperature. Such an assumption is of great value as it is then possible to consider the mechanism of the oxidation processes of ethylbenzene in the light of contemporary ideas on the peroxide theory of oxidation and theory of radical-chain processes. The scheme given for the main directions of ethylbenzene oxidation takes into consideration these data and explains quite well all the reaction mechanisms noted above.



The formation of ethylbenzene hydroperoxide (II) should be considered as the initial stage of the process. The subsequent stages are determined by the direction of the decomposition of this hydroperoxide. According to literature data [4], secondary unsymmetrical hydroperoxides may decompose in three directions. When the hydroperoxide (II) decomposes with the elimination of a water molecule, the subsequent intermediate reaction product would be acetophenone (III). When this is oxidized, it gives first phenylglyoxal (IV) and then benzoic acid (V). The benzoic acid is first decarboxylated. The phenyl radical thus formed may give benzene (VI) or may possibly react directly with oxygen. In both cases the reaction results in the formation of maleic anhydride (X). The intermediate products at this stage are, as we showed previously [5], phenol (VII), hydroquinone (VIII) and quinone (IX).

Another possible direction of decomposition of ethylbenzene hydroperoxide is characterized by the elimination of a methyl alcohol molecule to form benzaldehyde (XI). Liquid phase oxidation of benzaldehyde, as is known [6], proceeds through the intermediate stage of benzoyl hydroperoxide and ends with benzoic acid formation. This reaction sequence also occurs in benzaldehyde gas phase oxidation. However, in this case, due to the relatively large intramolecular distances and drastic temperature conditions, the monomolecular decarbonylation of benzaldehyde and decarboxylation of its hydroperoxide (XII) acquired considerable importance. From the point of view of radical-chain processes, these reactions may be written in the following way:



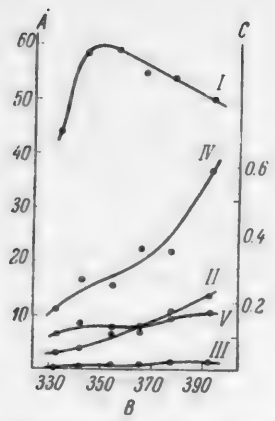


Fig. 2. Benzaldehyde oxidation. A) Yield of incomplete oxidation products (in %), B) reaction temperature, C) CO and CO_2 yield (in moles per mole of benzaldehyde passed). I) Benzoic acid, II) maleic anhydride, II) quinone, IV) CO, V) CO_2.

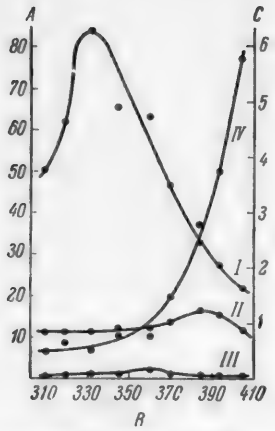


Fig. 3. Acetophenone oxidation. A) Yield of incomplete oxidation products (in %), B) reaction temperature, C) CO_2 yield (in moles per mole of acetophenone passed). I) Benzoic acid, II) maleic anhydride, III) quinone, IV) CO_2.

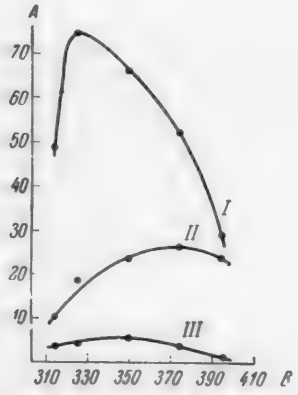


Fig. 4. Phenylglyoxal oxidation. A) Yield of incomplete oxidation products (in %), B) reaction temperature. I) Benzoic acid, II) maleic anhydride, III) quinone.

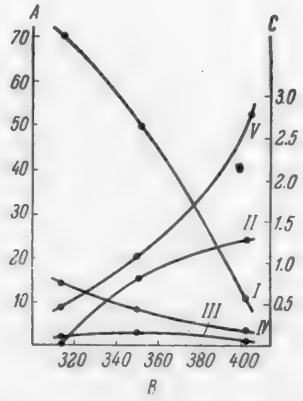


Fig. 5. Benzoic acid oxidation. A) Yield of incomplete oxidation products (in %), B) reaction temperature, C) CO and CO_2 yield (in moles per mole of benzoic acid passed). I) Unreacted benzoic acid (in %), II) maleic anhydride, III) quinone, IV) CO, V) CO_2.

The relatively large amounts of carbon monoxide detected in the benzaldehyde and ethylbenzene experiments indicate that benzaldehyde decarbonylation plays a very important role in ethylbenzene oxidation. Both it and benzaldehyde hydroperoxide decarboxylation are among the side reactions which hinder benzoic acid formation.

The last of the three directions of ethylbenzene hydroperoxide decomposition should also be examined as a side reaction in ethylbenzene oxidation and this involves the rupture of the bond between the carbon atoms of the aromatic ring and the side chain. In this case, as in the others, the phenyl radical is finally converted to maleic anhydride.

The scheme of the process was also confirmed by the analytical data on the gaseous reaction products. Figs. 1 and 2-5 show that in all the experiments carried out at temperatures below 350-370°, the products of incomplete ethylbenzene oxidation were mainly formed. However, the amount of complete oxidation products produced corresponded almost exactly (calculated on the CO_2) to the scheme:

$$\text{Ethylbenzene} \xrightarrow{-CO_2} \text{Benzoic acid} \xrightarrow{-CO_2} \text{Quinone} \xrightarrow{-2CO_2} \text{Maleic anhydride.}$$

Such a mechanism is quite natural as in this series of substances, maleic anhydride is the only compound which gives only an end reaction product when oxidized [5] and is quite stable under the given conditions. With rising temperature, the stability of the incomplete oxidation products decreased and they were converted more rapidly in all the stages and even the maleic anhydride was oxidized. In fact, at a temperature of 350-390°, the yield of incomplete oxidation products decreased as a rule and, at the same time, considerable evolution of CO and CO_2 began. Extensive oxidation became the predominating process above 390-410°.

EXPERIMENTAL

The characteristics of the materials taken for oxidation are given in the table.

Oxidizable material	Melting point	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	Comments
Ethylbenzene	—	133.5° (697)	1.4954	0.8663	—
Acetophenone	19°	199.5—200 (704)	1.5340	1.0250	—
Benzaldehyde	—	176 (700)	1.5459	1.0511	Contained 3.1% of benzoic acid
Phenylglyoxal	87—88	—	—	—	Contained 6.5% of benzoylformic acid
Benzoic acid	121	—	—	—	Neutralization equivalent, 121.1

The oxidation of ethylbenzene and the other compounds was carried out in an all-metal reactor of the flow type, with a stainless steel reaction tube, 1100 mm long and 20 mm in diameter, heated with an electric furnace. The apparatus for the steady input of the starting materials into the reaction chamber and the system of trapping the solid reaction products were described in our previous papers [7, 8]. Granulated tin vanadate, in the form of grains 3-5 mm across, was used as the catalyst. Moist air, with a water content of 350 g/m^3, was used as the oxidant. The experiments were performed with a contact time of 0.3-0.4 sec., the starting product input rate was 5-6 g/hour and the ratio of oxidizable material to air was 1 : 65 — 1 : 75. Only the reaction temperature was varied. The solid and liquid reaction products were identified and determined quantitatively by the methods described in previous papers [5, 9, 10]. The composition of the gaseous reaction products was determined using a VTI (All-Union Heat Engineering Institute) apparatus; the CO_2 determination was duplicated by absorbing it in barium hydroxide solution and the CO was determined in parallel by the hopcalite method [11].

Oxidation of ethylbenzene. Eight experiments were performed at temperatures from 310-410°. The temperature dependence of the main reaction products is shown in Fig. 1. At temperatures of 310-355°, benzaldehyde and acetophenone were detected among the reaction products. The yield of neither of these exceeded 2-3%. In all cases, qualitative reactions proved the presence of phenol, hydroquinone and formaldehyde. In two experiments carried out at 270-280° with freezing of the reaction products, the formation of peroxide compounds was demonstrated qualitatively.

Oxidation of benzaldehyde. The yields of the main products at different temperatures are shown in Fig. 2. In addition, we found 2.5 and 1% (respectively) of unreacted starting material in the first two experiments of this series. Qualitative reactions demonstrated the presence of phenol, hydroquinone and formaldehyde.

Oxidation of acetophenone. The yields of the main reaction products at different temperatures are shown in Fig. 3. In comparison with the other oxidized materials, acetophenone gave the greatest quantity

of benzoic acid. At 332°, the yield of the latter was 85%. Among the oxidation products, we found phenol, hydroquinone and formaldehyde in all the experiments. Benzaldehyde was not found.

Oxidation of phenylglyoxal.* This compound was not found in the oxidation of ethylbenzene, despite the fact that it was considered as one of the probable intermediates of this reaction. As with acetophenone, phenylglyoxal was found to be extremely oxidizable. It reacted completely even at 320° (Fig. 4), when the maximum total yield of products of incomplete oxidation was 97%. Qualitative reactions for phenol, hydroquinone and formaldehyde were positive in all the experiments. Benzaldehyde was not found among the oxidation products. The CO and CO_2 were not determined.

Oxidation of benzoic acid. The products of incomplete oxidation in this case were phenol, quinone, maleic anhydride and CO and of these phenol was determined only qualitatively. At 350° about 50% of unreacted benzoic acid passed through the reaction chamber (Fig. 5) and this indicates its relatively high stability. To find the benzene in the products of benzoic acid oxidation, we carried out special experiments, in which the emergent gases were first frozen with liquid air and then passed through traps with activated charcoal and silica gel. Benzene could not be found by this method.

SUMMARY

1. We studied the vapor phase oxidation of ethylbenzene with moist air in the presence of tin vanadate. The oxidation of the intermediate products of this reaction was studied under comparable conditions.

2. A scheme for the main directions of the vapor phase oxidation of ethylbenzene over tin vanadate was put forward based on data from the peroxide theory of oxidation and the theory of radical-chain processes.

3. A hypothesis was put forward that ethylbenzene oxidation may proceed simultaneously in several parallel directions, both main and side processes. Each one of them is a multistage process of gradual destruction of the initial substances' carbon skeleton followed by the formation of numerous intermediate products. The final stage of each process is the formation of the products of complete oxidation.

LITERATURE CITED

[1] E. B. Maxted, J. Soc. Chem. Ind. 47, 101 (1928).

[2] K. I. Ivanov, J. Gen. Chem. 6, 470 (1936).

[3] V. Ia. Shtern, Chain Oxidation of Hydrocarbons in the Gas Phase, Acad. Sci. USSR Press, 37 (1955).**

[4] K. I. Ivanov, Intermediate Products and Intermediate Reactions of Hydrocarbon Autooxidation, State Tech. Theor. Press (1949).**

[5] S. R. Rafikov, B. V. Suvorov and A. V. Solomin, Bull. Acad. Sci. Kazan SSR (Chem. series) No. 11, 98 (1956).

[6] D. Swern, Chem. Revs. 45, 1 (1949).

[7] B. V. Suvorov and S. R. Rafikov, Fact. Labs. 18, 764 (1952).

[8] B. V. Suvorov and S. R. Rafikov, Fact. Labs. 18, 891 (1952).

[9] B. V. Suvorov, S. R. Rafikov and I. G. Anuchina, Proc. Acad. Sci. USSR, 88, 79 (1953).

[10] S. R. Rafikov and B. V. Suvorov, Bull. Acad. Sci. Kazan SSR (Chem. series), No. 5, 86 (1953).

[11] B. G. Eremina, Gas Analysis, State Chem. Press, 118 (1955).**

[12] Synth. Org. Prep. Coll. 2, Foreign Lit. 507 (1951) [Russian Trans.].

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*Prepared by the method described by Riley and Gray [12].

**In Russian.

SYNTHESIS, PROPERTIES AND POLYMERIZATION OF α-CHLOROACRYLAMIDE

S. S. Ivanov and M. M. Koton

The amides of some acids of the acryl series may be prepared by a general method: by treating the appropriate esters with aqueous ammonia. Using this method, Arcus [1] prepared methacrylamide in good yield by shaking methyl methacrylate with excess concentrated ammonia in the cold.

α-Chloroacrylamide could not be synthesized by this method as, besides the substitution of the methoxyl group by the amide group, chlorine was eliminated. The authors of a French patent [2] report that α-chloroacrylamide may be prepared by hydrolyzing α-chloroacrylonitrile with sulfuric acid. However, this patent does not describe the method of isolating the α-chloroacrylamide from the reaction mixture and ways of purifying it and the characteristics given for the monomer itself are quite insufficient (only its m. p. of 93° is given).

We prepared α-chloroacrylamide in the same way by hydrolyzing α-chloroacrylonitrile (I) with sulfuric acid, in order to study its capacity for polymerization.

$$\underset{\text{(I)}}{CH_2{=}CCl{-}CN} \xrightarrow[H_2SO_4]{HOH} \underset{\text{(II)}}{CH_2{=}CClCONH_2}$$

The α-chloroacrylonitrile (I) was synthesized by dehydrochlorinating α, β-dichloropropionitrile with sodium acetate [3] and the α, β-dichloropropionitrile by chlorinating acrylonitrile in the presence of pyridine [3].

EXPERIMENTAL

Synthesis of α, β-dichloropropionitrile. Chlorine was passed into 53 g of acrylonitrile with 14 g of pyridine, cooled with water, for 3 hours until the reaction mixture had increased in weight by 71 g. The reaction product was shaken with distilled water in a separating funnel, dried with calcium chloride and distilled in vacuum at 61° (13 mm). We obtained 117.8 g (95%) of α, β-dichloropropionitrile as a colorless, lachrimatory liquid with a sharp smell, which was soluble in benzene, alcohol, dioxane and chloroform: d_4^{20} 1.338, n_D^{20} 1.4645 [3].

Found %: C 29.01; H 2.67; N 11.28; Cl 57.17. $C_3H_3NCl_2$. Calculated %: C 29.05; H 2.44; N 11.30; Cl 57.22.

Synthesis of α-chloroacrylonitrile (I). 56 grams of α, β-dichloropropionitrile, 50 ml of methyl alcohol and 60 g of sodium acetate were placed in a flask with a reflux condenser. The mixture was heated for 2 hours at 65°, washed with distilled water and the precipitated oil separated and dried with calcium chloride. Distillation on a column with copper packing in the presence of hydroquinone at atmospheric pressure gave 26.5 g (67%) of α-chloroacrylonitrile.

B. p. 87° (755 mm), 73° (726 mm), d_4^{20} 1.06, n_D^{20} 1.4301 [3].

The α-chloroacrylonitrile was a colorless, lachrimatory liquid with a sharp smell, which was soluble in benzene, dioxane, ether and chloroform.

Found %: C 41.03; H 2.42; N 15.92; Cl 40.47. C_3H_2NCl. Calculated %: C 41.15; H 2.30; N 16.01; Cl 40.57.

Synthesis of α-chloroacrylamide (II). 25.0 g of α-chloroacrylonitrile, 56.6 g of 85% sulfuric acid and 0.1 g of hydroquinone were placed in a 150 ml, thick-walled pyrex flask, fitted with a stirrer. The reaction mixture was stirred for 2 hours at 0°, 20 hours at 25°, 12 hours at 40° and 2 hours at 60° and then neutralized with a saturated solution of sodium bicarbonate after cooling in ice. The precipitated sodium sulfate crystals were separated and extracted 3 times with ether in portions of 100 ml each. The neutralized reaction mixture, whose volume usually did not exceed 350-500 ml, was shaken with equal volumes of ether until the α-chloroacrylamide was completely extracted. The ether extracts were combined and the ether evaporated off at room temperature in vacuum.

TABLE 1

Solubility of α-Chloroacrylamide at 20°•

Solvent	α-Chloroacrylamide (g) dissolved in 100 ml solvent
Acetone	94.70
Methanol	72.68
Ethanol	31.11
Ether	18.82
Chloroform	7.29
Carbon tetrachloride	7.26
Water	6.50
Benzene	3.76
Toluene	2.68

We obtained 18.5 g (61.4%) of α-chloroacrylamide with m. p. 90-94°. After recrystallization from benzene twice to remove traces of hydroquinone, the crystals of α-chloroacrylamide appeared as white plates with m. p. 94°. They decolorized a solution of bromine in acetic acid on heating, did not give a reaction for chlorine with $AgNO_3$ and gave off ammonia on boiling with concentrated alkali.

Found %: C 34.19; H 3.90; N 13.27; Cl 33.80. M (cryoscopic) 104.5; MR 22.48. C_3H_4ONCl. Calculated %: C 34.12; H 3.79; N 13.27; Cl 33.60. M 105.5; MR 23.06.

The crystals of α-chloroacrylamide were not very stable and on long storage (for more than a month) under normal conditions, they gradually decomposed with the loss of chlorine and nitrogen and a decrease in solubility and showed a double molecular weight in cryoscopic determinations. If solutions of α-chloroacrylamide fell onto the skin, they produced burns and blisters appeared.

• The solubility of α-chloroacrylamide was determined by the method described by Meier [4].

At room temperature, α-chloroacrylamide was readily soluble in water, methyl and ethyl alcohols, acetone and ether and less soluble in benzene and toluene. Data on the solubility of α-chloroacrylamide is given in Table 1.

Bromination. The bromination of α-chloroacrylamide at room temperature occurred to a very small degree, even on keeping the reaction mixture in the dark for several days. On heating the material with a considerable excess of bromide – bromate mixture, the bromination went to completion.

The action of concentrated aqueous ammonia on α-chloroacrylamide. 1.0386 g of α-chloroacrylamide, dissolved in 100 ml of concentrated ammonia, was left to stand at room temperature for 7 days. The excess ammonia was evaporated off at room temperature in vacuum, when crystals of ammonium chloride were deposited (0.5632 g, 96.5%) and these were collected on a Schott filter.

Found %: Cl 66.26. NH_4Cl. Calculated %: Cl 66.30.

Traces of ammonium chloride were removed by several solutions in water and precipitations with methanol (test with $AgNO_3$).

An attempt to isolate the amide of pyruvic acid (m. p. 124-125°) by extraction of the tarry precipitate formed with chloroform and hot benzene [5] gave negative results. After drying in vacuum at room temperature , the tarry precipitate formed a clear, friable film of polymer, which was brown in color and had strong adhesion to glass. The polymer was readily soluble in water and was precipitated by methyl alcohol.

Found %: C 41.17; H 5.61; N 15.75. M 528. $(C_3H_3O_2N)_n$. Calculated %: C 41.38; H 5.75; N 16.10. M 87 (n = 6).

Polymerization of α-chloroacrylamide proceeded in block (in an atmosphere of air or nitrogen) in benzene solution in the presence of benzoyl peroxide and azoisobutyrodinitrile (0.2%) and also in an aqueous solution with hydrogen peroxide[1] and with potassium persulfate (0.02 mole%). The samples of block polymers, which were brown in color, were carefully powdered and washed with benzene and ether to remove monomer and initiator and then with distilled water until the Cl' was completely removed (reaction with $AgNO_3$).

The polymers obtained in benzene were treated as described above, after removal of the solvent, and after drying they formed white powders. These polymers were insoluble in water and the usual organic solvents (alcohols, acetone, ether, benzene, chloroform, dioxane, carbon tetrachloride, ethyl acetate, nitrobenzene and ammonia) both in the cold and on heating. In both cases the aqueous solutions, after washing the polymers, yielded variable amounts of ammonium chloride (from 3.3 to 8.8%), equivalent to the nitrogen liberated from the polymers. The polymerization in aqueous solutions with hydrogen peroxide and potassium persulfate began after several minutes at room temperature with the formation of a flocculent polymer. The addition of methanol to the aqueous solutions gave brown polymers which were readily soluble in water, slightly soluble in hot dimethylformamide and completely insoluble in the usual organic solvents and also pyridine, aniline, acetic anhydride and concentrated sulfuric acid. They swelled in hot nitrobenzene and in this state they could be formed into fibers and films [2]. On heating above 200° for 10 hours, the polymers lost their solubility in water, cross-linking like other thermosetting polymers. Data on the polymerization of α-chloroacrylamide is given in Table 2.

DISCUSSION OF RESULTS

On polymerizing α-chloroacrylamide we observed a noticeable decrease in the chlorine content and, to a lesser degree, in the nitrogen content of the polymers as compared with the content of the initial monomer; certain differences in the polymer composition were due to the nature of the polymerization initiators used (Table 2). Apparently, the elimination of chlorine and nitrogen cannot be explained by the thermal instability of the monomer as when α-chloroacrylamide was heated above its melting point (93-94°) there was resinification only in the temperature range 135-170°.

TABLE 2

α-Chloroacrylamide Polymerization

Polymerization conditions	Initiator	Time (hrs)	Temperature	Yield (%)	Content (%)	
					N	Cl
In block •	Benzoyl peroxide	36	100°	76.4	11.8	16.2
In block •	Azoisobutyrodinitrile	18	100	90.0	11.2	23.2
In block••	Benzoyl peroxide	24	100	70.5	10.2	18.3
In block••	Azoisobutyrodinitrile	18	100	76.0	11.3	23.8
In a solution of C_6H_6	Benzoyl peroxide	18	60	96.1	12.5	23.9
In a solution of C_6H_6	Azoisobutyrodinitrile	18	60	91.7	11.3	31.0
In a solution of H_2O•••	H_2O_2	18	60	84.5	6.5	3.8
In a solution of H_2O•••	$K_2S_2O_8$	—	—	98.7	2.6	1.8
Pyrolysis product••••	—	10	200	—	4.5	0.1
α-Chloroacrylamide	—	—	—	—	13.27	33.65

•In air.

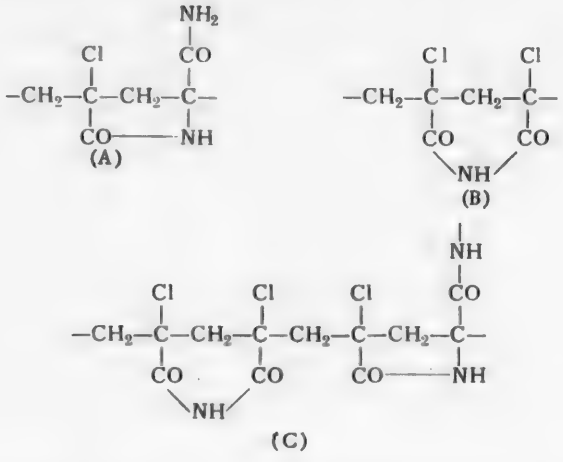
••In an atmosphere of nitrogen.

•••Molecular weight (cryoscopic): 290.3 (with H_2O_2) and 400.0 (with $K_2S_2O_8$).

••••Polymer, obtained from H_2O_2.

[1]Into the ampule was placed several drops of concentrated aqueous ammonia.

The liberation of ammonium chloride in α-chloroacrylamide polymerization indicated the existence of secondary reactions proceeding during the polymerization and accompanied by the elimination of chlorine (in the form of HCl) and nitrogen (in the form of NH_3). Apparently, at the same time both in block and in a benzene solution cyclic polymer units of the type (A) and (B) are formed and due to secondary reactions they form cellular (cross-linked), insoluble structures of type (C).



In aqueous solutions α-chloroacrylamide polymerized with the substitution of chlorine by hydroxyl from the water and partial hydrolysis of the amide group, catalyzed by the hydrogen chloride evolved. Heating such water soluble polymers above 200° resulted in the elimination of the elements of water to give cross-linked polymers.

SUMMARY

1. We describe a method of synthesizing, isolating and purifying α-chloroacrylamide.

2. Some of the properties of α-chloroacrylamide and its polymer were characterized.

3. It was shown that treatment of α-chloroacrylamide with concentrated aqueous ammonia at room temperature resulted in chlorine elimination and the formation of a polymer of low molecular weight.

4. It was shown that α-chloroacrylamide polymerization proceeded with nitrogen and chlorine elimination to form cross-linked polymers in block or in a benzene solution. In an aqueous solution, a partially hydrolyzed poly-α-hydroxyacrylamide was formed, which was soluble in water.

LITERATURE CITED

[1] C. L. Arcus, J. Am. Chem. Soc. 71, 2732 (1949).

[2] Fr. Patent 1041375 (1953); Zbl. 1954, 7996.

[3] H. Brintzinger, K. Pfannstiel and H. Koddebusch, J. Angew. Chem. A 60, No. 11-12, 311 (1948).

[4] G. Meier, Analysis and Determination of the Structure of Organic Compounds, 80 (1935).

[5] L. Claisen and J. Shadwell, Ber. 11, 1566 (1878).

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A STUDY OF THE CHEMICAL STRUCTURE OF THE SPONGY DIVINYL POLYMER. II.

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We had previously [1] established that the ozonolysis products of spongy divinyl polymer contained formic, succinic, butane-1,2,4-tricarboxylic and hexane-1,x,y,6-tetracarboxylic acids.* This indicated that the spongy divinyl polymer contained the same sections as were found in the ozonolysis products of divinyl caoutchoucs, prepared under various conditions [2], namely: 1) formed by units with an internal double bond which was repeated at least 2 times in succession, 2) sections in which a unit with an external double bond was enclosed by units with an internal double bond, and 3) sections in which 2 units with an external double bond were enclosed by units with an internal double bond.** Kahrach [3] put forward the hypothesis that this polymer was a cross-linked polymer. As we found no substances in the ozonolysis products of the spongy polymer which would have indicated a steric structure, in this work we investigated more fully the ozonolysis products of the spongy divinyl polymer, changing the conditions under which they were isolated. In the previous work [1] the acid ozonolysis products were converted to methyl esters, which were separated by fractional distillation.

In the present work we separated the acids by partition chromatography which made it possible to separate the acids more precisely, as they differed very little in structure and molecular weight, and to detect them, even if they were in minute quantities.

The decomposition products of the ozonide of the spongy divinyl polymer contained, besides succinic, butane-1,2,4-tricarboxylic and hexane-1,x,y,6-tetracarboxylic acids, propane-1,2,3-tricarboxylic and levulinic acids. Also, it can be assumed that peak II on chromatogram 1 (Fig. 1) corresponded to propionic acid.***

The propionic acid could have been formed from the section -1,4-1,4- by anomalous ozonolysis. Propane-1,2,3-tricarboxylic acid could have been formed during the oxonolysis of the branched or cross-linked section formed in the transfer of the chain by the α-methylene group in the -1,4-1,4- section. Marvel [5] put forward the hypothesis that the propane-1,2,3-tricarboxylic acid could be the anomalous product of the ozonolysis of sections -1,4-1,2-1,4-, or could be formed from the section -1,4-1,4- at the branching at the α-methylene groups, as the spongy divinyl polymer has a considerable number of α-methylene groups.

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*The ozonolysis products may contain three isomeric hexanetetracarboxylic acids: hexane-1,2,4,6-tetracarboxylic, hexane-1,3,5,6-tetracarboxylic and hexane-1,2,5,6-tetracarboyxlic acids [4], formed from the sections: 1,4-1,2-1,2-1,4-, -1,4-1,2-2,1-1,4-,-1,4-2,1-1,2-1,4-.

**Units, formed by adding divinyl at the 1,4-position are called units with an internal double bond (I) and those formed by addition at the 1,2 position – units with an external double bond (II).

$$\underset{\text{(I)}}{-CH_2-CH=CH-CH_2-} \qquad \underset{\text{(II)}}{-CH_2-\underset{\displaystyle CH=CH_2}{\underset{|}{CH}}-}$$

***As shown by work carried out in our laboratory.

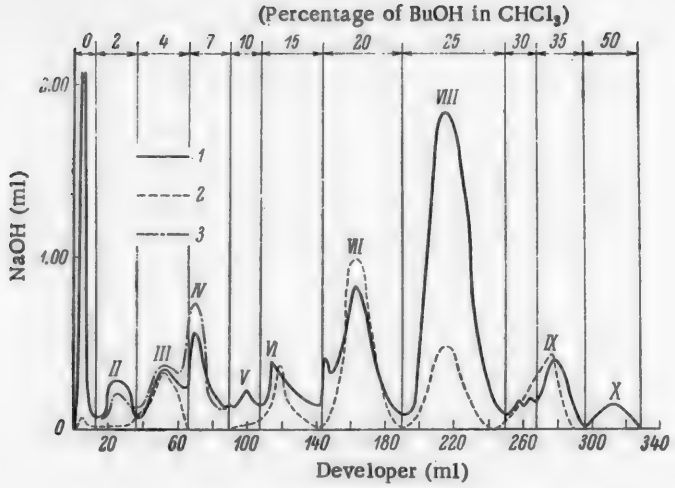

Fig. 1. 1) Partition chromatogram of liquid acids, 2) partition chromatogram of standard acid mixture, 3) partition chromatogram of liquid acids with levulinic and acetic acids added. Explanation in the text.

The levulinic acid could have been formed by the scheme

$$-CH_2-CH=CH-CH_2-\underset{\displaystyle CH=CH_2}{\underset{|}{CH}}-CH_2-CH_2-CH=CH-CH_2- + R\cdot \rightarrow$$

$$\rightarrow -CH_2-CH=CH-CH_2-\underset{\displaystyle CH=CH_2}{\underset{|}{\dot{C}}}-CH_2-CH_2-CH=CH-CH_2- + RH \rightarrow$$

$$\rightarrow -CH_2-CH=CH-CH_2-\underset{\displaystyle CH-\dot{C}H_2}{\underset{\|}{C}}-CH_2-CH_2-CH=CH-CH_2- \quad [2,5]$$

Figures 1 and 2 show the chromatograms obtained by the separation of the acids isolated from the ozonolysis products of the spongy divinyl polymer. We calculated from the chromatograms the percentage of polymer carbon skeleton in the acids and in the sections. The calculation results are given in Tables 1 and 2.

The oxidative decomposition products of the ozonide of the spongy divinyl polymer contained 74.4% of the carbon skeleton of the ozonized polyer. Of it, 68.7% was in the acids identified (see Fig. 1, peaks II, III, VII, VIII, IX, X; Fig. 2, peaks III, V, VI, VII) and 5.6% of the polymer carbon skeleton was in the acids of undetermined structure, which corresponded to peaks I and V in chromatogram 1 (Fig. 1). Besides that, chromatogram 1 had peaks which corresponded to acetic and formic acids.

Sections were found in the spongy divinyl polymer, which has no caoutchouc-like properties, that had the same structure as in divinyl caoutchoucs. As the properties of compounds with high molecular weight are determined not only by the chemical structure but also by the shape and size of the molecules and their relative position and interaction, it is possible that the spongy divinyl polymer consists of linear macromolecules, joined in bunches by an insoluble nucleus. The presence of a primer, introduced preliminarily or formed during polymerization, is a prerequisite condition for the formation of a divinyl autopolymer [6, 7].

TABLE 1

Name of acid	Percentage of polymer carbon skeleton in the acid
Propionic	1.00
Levulinic	4.93
Succinic	39.74
Butane-1,2,4-tricarboxylic	14.96
Propane-1,2,3-tricarboxylic	1.83
Hexane-1,x,y,6-tetracarboxylic	1.18

TABLE 2

Name of acid	Structure of polymer section	Polymer carbon skeleton in section (%)	Percentage	
			1,4	1,2
Propionic	—1,4—1,4—	1.00	1.00	—
Levulinic	—1,4—1,2—1,4—	7.89	3.95	3.95
Succinic	—1,4—1,4—	39.74	39.74	—
Butane-1,2,4-tricarboxylic	—1,4—1,2—1,4—	17.10	8.55	8.55
Propane-1,2,3-tricarboxylic	—1,4—1,4—	1.83	1.83	—
Hexane-1,x,y,6-tetracarboxylic	—1,4—(—1,2—)$_2$—1,4—	1.18	0.39	0.78
		68.74	55.46	13.28

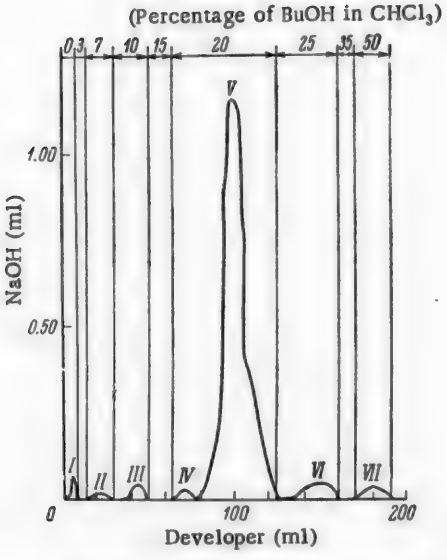

Fig. 2. Partition chromatogram of crystalline acids. Explanation in the text.

EXPERIMENTAL

The spongy polymer of divinyl was isolated from the autopolymer of divinyl, which was prepared by the slow polymerization of divinyl at 15-20° over a period of two years. The autopolymer of divinyl was readily oxidized in air and therefore all the work on the separation of the divinyl dimer and the soluble divinyl polymer and the isolation of the spongy divinyl polymer was carried out in an atmosphere of nitrogen [1].

Found %: C 88.15, 88.15; H 11.19, 11.12. $(C_4H_6)_x$. Calculated %: C 88.89, H 11.11.

Twelve g of spongy divinyl polymer, containing 10.58 g of carbon, was ozonized in ethyl acetate at -30°. The ozonide obtained was soluble in ethyl acetate. The solvent was distilled off from the polymer at 18 mm and 20°. The ozonide was dissolved in glacial acetic acid and decomposed with acetyl hydroperoxide. The excess acetyl hydroperoxide was destroyed with platinum black. The acetic acid was distilled off from the products of oxidative decomposition of the ozonide at 4 mm until the acids reached constant weight. We obtained 18.86 g of liquid and crystalline acids. The crystalline acids

were separated from the liquid with diethyl ether. After removal of the diethyl ether, we obtained 8.51 g of liquid acids containing 3.72 g of carbon, and 10.35 g of crystalline acids containing 4.15 g of carbon. The acids obtained contained 7.87 g of carbon or 74.4% of the carbon skeleton of the polymer.

Found %: C 43.46, 43.88; H 5.09, 5.43.

The loss of polymer carbon skeleton during the oxidative decomposition of the ozonide with acetyl hydroperoxide was 2.71 g or 25.6%.*

After recrystallization from hot water, the crystalline acids melted at 183°, and a mixture with succinic acid (m. p. 183°) melted at 183°. The neutralization equivalent of the succinic acid isolated was determined as 59.

As the support for partition chromatography for separation of the acids, we used silica gel of MSK (fine silica gel of coarse porosity) grade of the Voskresenskii Chemical Combine [8]. As the stationary solvent we used water and for the mobile one, a mixture of chloroform and butyl alcohol, first saturated with water. In a column 480 mm long and 19 mm in diameter, we placed 25 g of silica gel (100-170 mesh), previously ground with 25 ml of water. The height of the silica gel layer in the column was 183 mm. The column was washed with chloroform to attain equilibrium on the surface. The mixture of liquid acids (0.9886 g) was dissolved in 10 ml of isoamyl alcohol. For the separation, 1.6 ml of the solution was taken with a pipette and introduced into the column carefully so that the surface of the silica gel was not disrupted. The acids were eluted from the column at a rate of 1 ml per minute with solutions of butanol in chloroform and titrated in 3 ml portions with a 0.0020 N solution of alkali in methyl alcohol. Phenolphthalein was used as the indicator. The polarity of the developer was gradually increased. The system of developers used was $CHCl_3$, 2, 4, 7, 10, 15, 20, 25, 30, 35, 50 % butanol in chloroform. From the chromatograms plotted from the titration data, we were able to calculate the amount of each acid in the mixture (Tables 4 and 5).

TABLE 3

	Peak volume of acids				
	levulinic	formic	succinic	butane-1,2,4-tricarboxylic	propane 1,2,3-tricarboxylic
In standard mixture of acids	52	119	165	214	272
In liquid acids	52	114	165	218	272

The chromatogram of the liquid acids is shown in Fig. 1 (chromatogram 1). The amount of alkali in milliliters, consumed in the titration of 3 ml of acid is plotted along the ordinate and the amount of developer in milliliters leaving the column along the abscissa.

To characterize the liquid acids we plotted a chromatogram of a mixture of those acids which we had previously found in the ozonolysis products of spongy divinyl polymer and also propane-1,2,3-tricarboxylic and levulinic acids, whose presence in the ozonolysis products might have been expected (Fig. 1, chromatogram 2). Later on this mixture of acids is refered to as the "standard" mixture of acids.

The composition of the standard mixture of acids (in g) was: formic 0.0023, levulinic 0.0106, succinic 0.0162, butane-1,2,4-tricarboxylic 0.0170 and propane-1,2,3-tricarboxylic 0.0085.

The separation of the "standard" mixture of the acids was performed with the same developer system as in the separation of the liquid acids obtained from the oxidative decomposition of the ozonide. The acids were identified by the peak volume [9].

*Part of the loss was due to HCOOH and the volatile products of anomalous ozonolysis. The spongy divinyl polymer contained 22.8% of the units 1,2 and therefore 5.7% of the carbon skeleton of the polyer was lost as HCOOH during the ozonolysis.

TABLE 4

Peak No. (Fig. 2)	Name of acid	Amount (mg)		Acids in crystalline acids (g)
		NaOH	acid in sample	
III	Levulinic	0.09	0.26	0.143
IV	Acetic	0.36	0.39	0.215
V	Succinic	12.15	17.23	9.380
VI	Butane-1,2,4-tricarboxylic	0.42	0.65	0.358
VII	Hexane-1,x,y,6-tetracarboxylic	0.25	0.24	0.135

Footnote: The weight of crystalline acids taken for the separation was 0.0190 g.

The peak volumes of levulinic, succinic and propane-1,2,3,4-tricarboxylic acids agreed with the peak volumes of the same acids in the standard mixture. The peak volumes of formic and butane-1,2,4-tricarboxylic acids disagreed slightly. This could have been the result of insufficient uniformity during development of the chromatograms; for example, differences in the flow rate of the mobile solvent. The order in which the acids emerged from the column was always preserved.

TABLE 5

Peak No. (Fig. 1)	Name of acid	Chromatogram 1 amount (mg)			Chromatogram 1a amount (mg)			Amount of acids in liquid acids isolated (g)
		NaOH	acids in sample	acids in 1 g of liquid acids	NaOH	acids in sample	acids in 1 g of liquid acids	
I	–	3.04	—	—	9.10	—	—	—
II	Propionic	2.27	4.2	25.1	1.97	3.64	23.4	0.206
III	Levulinic	4.30	12.5	76.9	4.65	13. 5	86.6	0.699
IV	Acetic	5.18	7.75	53.1	3.45	5.10	47.6	0.427
V	–	1.64	—	—	1.71	—	—	—
VI	Formic	4.48	5.15	31.6	3.90	4.48	28.8	0.256
VII	Succinic	12.17	17.82	114.9	12.17	17.82	114.9	0.956
VIII	Butane-1,2,4-tricarboxylic	36.20	57.20	351.8	34.2	54.20	348.5	2.975
IX	Propane-1,2,3-tricarboxylic	6.12	8.96	56.5	5.98	8.78	55.10	0.475
X	Hexane-1,x,y,6-tetracarboxylic	1.15	1.87	11.5	0.90	1.51	9.80	0.091

Footnote: Weight of liquid acids taken for the separation, 0.1626, 0.1553 g. Chromatogram 1 was similar to chromatogram 1a.

The oxidative decomposition of the ozonide of the spongy divinyl polymer was carried out in glacial acetic acid and therefore, the presence of the latter in the liquid acids was unavoidable. In order to prove which of the peaks on chromatogram 1 corresponded to acetic acid, acetic and levulinic acids were added to a solution of the liquid acids and chromatogram 3 (Fig. 1) plotted and from this it was obvious that acetic acid corresponded to peak IV and levulinic to peak III.

Thus, on the chromatogram of the liquid acids, isolated from the products of oxidative decomposition of the ozonide of spongy divinyl polymer, peak II corresponded to propionic acid,* peak III – levulinic acid, peak IV – acetic acid, peak VI – formic, peak VII – succinic, peak VIII – butane-1,2,4-tricarboxylic, peak IX – propane-1,2,3-tricarboxylic, peak X – hexane-1,x,y,6-tetracarboxylic acids.* The first peak may contain acid esters of the acids as the latter were dissolved in tertiary amyl alcohol. In addition, Stoll [10] showed that in the ozonization of ethylene compounds in ethyl acetate, esters of the acids were found. If we assume that an analogous process occurs in the ozonolysis of caoutchoucs in ethyl acetate also, then the esters thus formed (neutral and acid) would contain carbon from the polymer skeleton, for which we had not allowed. The nature of the acid in peak VI was not established, but hypothetically it could have been glutaric acid, which could have been formed by the anomalous ozonolysis of a portion -1,4-1,2-1,4-, similar to the formation of glutaric acid observed by Zigler [11] in the ozonolysis of cyclohexene.

The separation of the crystalline acids, isolated from the ozonolysis of spongy divinyl polymer, was carried out with same system of developers.

Among the crystalline acids, succinic acid predominated and emerged on washing the column with a 20% mixture of butanol in chloroform (91.1% of the acids taken for analysis); the other acids were present in very small amounts. There were no other acids in the acetic acid distilled from the decomposition products of the ozonide. The results of the calculation of the amount of acids, found in the products of oxidative decomposition of the ozonide of spongy divinyl polymer, from the chromatograms for the separation of the liquid and crystalline acids are given in Tables 4 and 5.

SUMMARY

1. Using partition chromatography, we established that the oxidative decomposition products of the ozonide of spongy divinyl polymer contained, in addition to the acids isolated previously [1], levulinic and propane-1,2,3-tricarboxylic acids.

2. Propane-1,2,3-tricarboxylic acid was formed from the sections of the spongy polymer macromolecules, branched at the α-methylene groups, and this confirms the mechanism for the formation of the spongy polymer, proposed by Kahrach [3].

LITERATURE CITED

[1] A. I. Iakubchik and A. I. Spasskova, J. Gen. Chem. 26, 1629 (1956).**

[2] A. I. Iakubchik, Academician S. V. Lebedev, Acad. Sci. USSR Press, 197 (1954).

[3] M. S. Kahrach and W. Nudenberg, Ind. Eng. Ch. 39, 7, 830 (1947).

[4] E. N. Alekseeva, J. Gen. Chem. 9, 1426 (1939).

[5] C. S. Marvel and Schilling, J. Org. Ch. 16, 838, 854 (1951).

[6] Devins and Winkler, Can. J. res. 26, 356 (1948).

[7] Welch, Ind. Eng. Ch. 39, 826 (1947).

[8] A. I. Iakubchik and S. K. Zykova, J. Appl. Chem. 29, 1591 (1956).**

[9] N. A. Fuks, Prog. Chem. 17, 45 (1948); 18, 206 (1949).

[10] Stoll and Ronve, Helv. Chim. Acta 27, 1950 (1944).

[11] Zigler, et al., Ann. Chem. 567, 99 (1950).

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*From the separation of the acids, obtained from the ozonolysis products of divinyl caoutchouc, it was established that the acid emerging on washing the column with 2% butanol was propionic and the acid emerging on washing the column with 50% butanol was hexane-1,x,y,6-tetracarboxylic acid.

**Original Russian pagination. See C. B. Translation.

CONDENSATION OF ω-BROMOACETOPHENONE WITH DIETHANOLAMINE

B. M. Mikhailov and A. N. Makarova

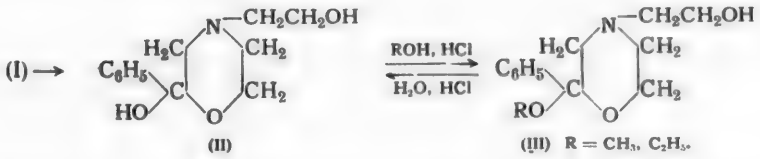
By mixing ω-chloroacetophenone with diethanolamine, Brighton and Reid [1] obtained a substance, with m. p. 44°, to which they assigned a chain structure and considered it as di-β-hydroxyethylaminoacetophenone (I). The authors did not investigate the chemical properties of the condensation product.

$$C_6H_5CO{-}CH_2Cl + NH(CH_2CH_2OH)_2 \rightarrow \underset{(I)}{C_6H_5COCH_2N(CH_2{-}CH_2OH)_2}$$

Later a series of authors [2-4] found that oxocyclotautomerism was inherent in such hydroxyamino ketones and that the equilibrium was displaced mainly towards the cyclic form. The condensation product of chloroacetone and diethanolamine also had a cyclic form, as we showed in a previous report [5].

In connection with this, it seemed interesting to study the properties of the condensation product of a ω-haloacetophenone with diethanolamine and to determine whether it actually has a chain structure, as put forward by Brighton and Reid, or whether it is a cyclic compound.

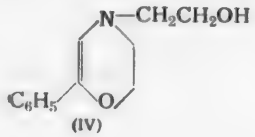
We prepared this substance by adding an ether solution of ω-bromoacetophenone to diethanolamine. The reaction proceeded quite smoothly and gave a good yield of a substance with m. p. 77-78°, and not 44°, as reported by Brighton and Reid. Investigation of the chemical properties of the substance obtained indicated that it was not a hydroxyamino ketone (I), but its tautomeric form, a cyclic semiacetal, 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine (II).



2-Phenyl-2-hydroxy-4-β-hydroxyethylmorpholine (II) was less stable than the corresponding 2-methyl compound [5]. When stored at room temperature it turned yellow and resinified. When recrystallized from water, the substance formed a molecular compound with water. The hydrate was unstable as it readily lost water when heated or in a vacuum desiccator. The semiacetal (II) hydrochloride, prepared by passing hydrogen chloride into an ether solution, reacted with anhydrous ethyl alcohol to give the hydrochloride of the acetal 2-phenyl-2-ethoxy-4-β-hydroxethylmorpholine (III, R = C_2H_5). The base was readily isolated from the salt by neutralizing it with an aqueous solution of potassium carbonate. The acetal hydrochloride (III, R = C_2H_5) was hydrolyzed to form the semiacetal (II) when heated in water for a short time at 70°. The semiacetal (II) hydrochloride was even more readily esterified with methyl alcohol. The acetal (III, R = CH_3) was isolated from its hydrochloride with potassium carbonate and characterized in the form of the methiodide and picrate.

The semiacetal (II) did not form a semicarbazone. When treated with semicarbazide it formed a solid substance with a high nitrogen content. The same nitrogenous substance was obtained by treating the acetal

(III, R = C_2H_5) with semicarbazide. However, the semiacetal (II) reacted with some reagents as a typical α-amino ketone. Thus, it rapidly reduced Fehling's solution and an ammonia solution of silver oxide at room temperature. Under these conditions, acetal (III) did not reduce Fehling's solution. When heated with concentrated hydrochloric acid in the semiacetal (II) eliminated water and was converted to 2-phenyl-4-β-hydroxyethyl-5,6-dihydrooxazine-1,4 (IV).



(IV)

EXPERIMENTAL

2-Phenyl-2-hydroxy-4-β-hydroxyethylmorpholine (II). Over a period of 1.5 hours, a solution of 10 g (0.05 mole) of ω-bromoacetophenone in 50 ml of absolute ether was added dropwise with stirring to 11.2 g (0.1 mole) of diethanolamine. During this time the temperature did not exceed 20-24°. The reaction mixture which consisted of two layers (the upper, slightly yellowish and the lower, thick and yellow), was left at room temperature overnight. Then, after boiling for 30 minutes, the ether layer a poured off from the thick mass and the latter extracted with ether. The ether was distilled off from the combined ether solutions. The residual oil crystallized on standing in the cold. The yield of 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine was 10.3 g (90.%). The m. p. was 72-74°. After two recrystallizations from benzene, the substance had m. p. 77-78°.

Found %: C 64.59; H 7.61; N 6.20; active H 0.85. $C_{12}H_{17}O_3N$. Calculated %: C 64.55; H 7.64; N 6.27 active 2H 0.90.

2-Phenyl-2-hydroxy-4-β-hydroxyethylmorpholine (II) was soluble in water, alcohols, benzene, acetone and chloroform; it was difficultly soluble in ether. The substance turned yellow and formed tar during storage at room temperature, but was stable to storage in the cold. It readily reduced an ammonia solution of silver oxide at room temperature (with the formation of a silver mirror) and Fehling's solution. Passing dry hydrogen chloride through an ether solution of 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine gave a flocculent precipitate of the hygroscopic hydrochloride.

2-Phenyl-2-hydroxy-4-β-hydroxyethylmorpholine hydrate. This was prepared by recrystallizing the substance (II) from water. The m. p. was 50-51°.

Found %: C 59.77; H 8.05; N 6.07; active H 1.21. $C_{12}H_{19}O_4N$. Calculated %: C 59.73; H 7.93; N 5.81; active 3H 1.25.

The hydrate dissolved readily in water, alcohol, acetone and ether. On being dried in vacuum for 0.5 hours, it lost water and was converted into substance (II).

The action of semicarbazide on 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine. A mixture of 1 g of 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine, 1.5 g of semicarbazide hydrochloride, 1.5 g of sodium acetate and 5 ml of water was boiled for 1 hour. The precipitate from the solution was recrystallized twice from dilute alcohol. The material obtained was a yellowish powder with m. p. 231-232° (decomp.). The material was very difficultly soluble in water and alcohols.

Found %: C 32.36; H 5.20; N 39.56.

2-Phenyl-2-ethoxy-4-β-hydroxyethylmorpholine hydrochloride. A mixture of the hydrochloride, prepared from 5 g of 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine, 20 ml of anhydrous ethyl alcohol and 1.2 ml of ethyl alcohol, saturated with hydrogen chloride, was boiled for 30 minutes. After distilling off 15 ml of alcohol, we added ether to the cooled residue until the solution became turbid. Crystals with m. p. 122-124° were isolated. The yield was 95%. After two recrystallizations from a mixture of alcohol and

ether, the substance had m. p. 125-126°. The hydrochloride of 2-phenyl-2-ethoxy-4-β-hydroxyethylmorpholine was readily soluble in water and alcohols.

Found %: C 58.21; H 7.67. $C_{14}H_{22}O_3NCl$. Calculated %: C 58.41; H 7.70.

2-Phenyl-2-ethoxy-4-β-hydroxyethylmorpholine (III, R = C_2H_5). An aqueous solution of 2-phenyl-2-ethoxy-4-β-hydroxyethylmorpholine hydrochloride was neutralized with potassium carbonate. The liberated base was extracted with ether and the extract dried over potassium carbonate. The ether was distilled off to leave an oil, which crystallized on cooling. The m. p. was 55-57°. The yield was 85%. After recrystallization from ethyl ether, benzene or a mixture of benzene and petroleum ether, the substance had m. p. 61.5-62.5°.

Found %: C 66.89; H 8.50; N 5.73; active H 0.45. $C_{14}H_{21}O_3N$. Calculated %: C 66.74; H 8.42; N 5.57; active H 0.40.

2-Phenyl-2-ethoxy-4-β-hydroxyethylmorpholine was very readily soluble in water and the usual organic solvents and did not reduce an ammonia solution of silver oxide at room temperature or Fehling's solution. On boiling 2-phenyl-2-ethoxy-4-β-hydroxyethylmorpholine with semicarbazide, we obtained the same substance as from the treatment of substance (II) with semicarbazide.

Hydrolysis of 2-phenyl-2-ethoxy-4-β-hydroxyethylmorpholine hydrochloride. An aqueous solution of 3.4 g of the hydrochloride was heated for 30 minutes at 70°. After cooling, the solution was neutralized with potassium carbonate and extracted with ether. The ether solution was dried over potassium carbonate. The ether was distilled off and the residual oil crystallized. The m. p. was 42-45°. The yield was 1.7 g (63%). After recrystallization from water, the substance had m. p. 50-51°. A mixed melting point of the substance obtained with 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine hydrate was not depressed.

2-Phenyl-2-methoxy-4-β-hydroxyethylmorpholine hydrochloride. On adding anhydrous methyl alcohol to 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine hydrochloride, we obtained a quantitative yield of 2-phenyl-2-methoxy-4-β-hydroxyethylmorpholine hydrochloride. After two recrystallizations from a mixture of methyl alcohol and ether, the substance formed lustrous plates with m. p. 142-143°. The hydrochloride was very readily soluble in water and alcohols.

Found %: C 57.14; H 7.38; N 13.06. $C_{13}H_{20}O_3NCl$. Calculated %: C 57.01; H 7.36; N 12.95.

2-Phenyl-2-methoxy-4-β-hydroxyethylmorpholine (III, R = CH_3). An aqueous solution of 2-phenyl-2-methoxy-4-β-hydroxyethylmorpholine hydrochloride was saturated with potassium carbonate. The base was extracted with ether. The ether solution was dried with potassium carbonate and then the solvent distilled off. An oily substance was obtained. The yield was 85%.

The methiodide had m. p. 159-160°, after recrystallization from alcohol.

Found %: C 44.15; H 5.93. $C_{14}H_{22}O_3NI$. Calculated %: C 44.33; H 5.85.

The picrate had m. p. 112-113°, after recrystallization from alcohol.

Found %: C 48.76; H 4.91; N 12.18. $C_{19}H_{22}O_{10}N_4$. Calculated %: C 48.93; H 4.76; N 12.02.

2-Phenyl-4-β-hydroxyethyl-5,6-dihydrooxazine (IV). 1.5 g of 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine was heated at 120° for 15 minutes. Then three drops of concentrated hydrochloric acid was added. The temperature rose to 160° at this. The thick, red-brown mass was distilled. We obtained 0.5 g of a substance with b. p. 185-188° (3 mm). The substance reacted with methyl iodide to give a methiodide, which was recrystallized from ethyl alcohol. The m. p. was 121-122°. The methiodide was readily soluble in alcohols and insoluble in ether.

Found %: C 44.78; H 5.22; N 3.96. $C_{13}H_{18}O_2NI$. Calculated %: C 44.96; H 5.22; N 4.03.

SUMMARY

1. ω-Bromoacetophenone reacted with diethanolamine to give a cyclic semiacetal, 2-phenyl-2-hydroxy--4-β-hydroxyethylmorpholine.

2. 2-Phenyl-2-hydroxy-4-β-hydroxyethylmorpholine esterified smoothly with alcohol. The alkoxyl derivative formed was readily hydrolyzed to the initial hydroxy compound.

3. 2-Phenyl-2-hydroxy-4-β-hydroxyethylmorpholine was dehydrated by heating to give 2-phenyl-4-β-hydroxyethyl-5,6-dihydrooxazine-1,4.

LITERATURE CITED

[1] K. W. Brighton and E. E. Reid, J. Am. Chem. Soc. 65, 479 (1943).

[2] N. Cromwell and K. Tsov, J. Am. Chem. Soc. 71, 993 (1949).

[3] R. Lutz and R. Jordan, J. Am. Chem. Soc. 71, 996 (1949).

[4] R. Jordan and R. Lutz, J. Am. Chem. Soc. 72, 1409 (1950).

[5] B. M. Mikhailov and A. N. Makarova, J. Gen. Chem. 27, 2526 (1957).*

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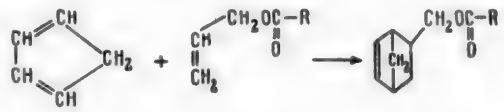
ORGANIC INSECTOFUNGICIDES

XXVIII. THE SYNTHESIS OF SOME ESTERS OF BICYCLO-(2,2,1)-HEPTENYL-5-CARBINOL-2*

S. S. Kukalenko and N. N. Mel'nikov

In recent years various polycyclic compounds, prepared by diene synthesis from cyclopentadiene and hexachlorocyclopentadiene have attracted the attention of investigators, as very active insecticides were found among them [1-6]. We undertook the synthesis of this type of compound in order to study the relation of the insecticide activity of the polycyclic compounds to their structure. First at all, we undertook the synthesis of various esters of bicyclo-(2,2,1)-heptenyl-5-carbinol-2 by reacting cyclopentadiene with allyl esters of various acids. The preparation of such derivatives is of doubtless interest as up to now the condensation of cyclopentadiene only with allyl alcohol, allyl chloride and bromide [7], some vinyl ethers [8], acrolein [9], acetylene [10, 11] and a small number of various other compounds [12, 13] has been described in the literature.

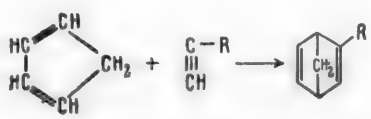
Cyclopentadiene reacted with the allyl esters of various acids at a high temperature in an autoclave or sealed tubes under some pressure, as with the reactions of cyclopentadiene with the majority of other unsaturated compounds. The reaction may be represented by the following general scheme:



R = CH_3, C_2H_5, C_3H_7, C_3H_7-uso, C_6H_5, CH_2Cl, CH_2SCN.

The compounds we prepared and their properties are listed in the table. As only the boiling points are given in the literature for the condensation products of cyclopentadiene with allyl alcohol and allyl bromide and chloride, we synthesized these products as well and also 2,3-dichlorobicyclo-(2,2,1)-heptene-5 from transdichloroethylene and cyclopentadiene.

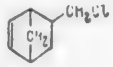
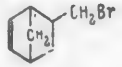
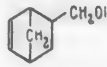
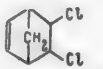
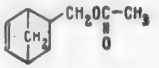
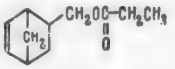
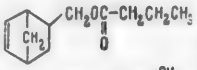
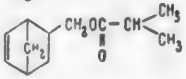
In order to prepare various arylbicyclo-(2,2,1)-heptadienes, we studied the reaction of cyclopentadiene with phenyl-, chlorophenyl-, bromophenyl- and tolylacetylenes. In this case we could expect reactions by the following scheme



*. R = C_6H_5, C_6H_4Cl, C_6H_4Br, $C_6H_4CH_3$.

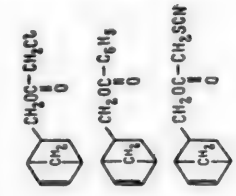
However, up to now we have not been able to isolate monomeric reaction products and isolated only solid polymeric substances with high molecular weights, whose structure has not yet been established.

*From S. S. Kukalenko's Candidate Thesis.

Substance No.	Formula	Yield (%)	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Analysis data (%) found C	found H	found Cl	calculated C	calculated H	calculated Cl
(I)*		49	51—52.5° (9)	1.070	1.4940	38.77	39.14	—	—	—	—	—	—
(II)*		58	77—79 (15)	1.370	1.5210	41.68	42.04	—	—	—	—	—	—
(III)*		42	67—70 (2.5)	1.040	1.5028	35.24	34.70	—	—	—	—	—	—
(IV)*		26.5	67—70 (8)	1.230	1.5110	39.70	39.39	—	—	—	—	—	—
(V)		60	83.5—84 (7)	1.035	1.4754	45.17	45.05	71.87, 71.79	8.99, 8.75	—	72.28	8.43	—
(VI)		59	98—100 (11)	1.033	1.4760	49.14	49.67	73.48, 73.26	8.99, 8.95	—	73.33	8.88	—
(VII)		56	114—115 (11—11.5)	1.016	1.4765	53.89	54.28	73.72, 73.74	9.27, 9.13	—	74.22	9.27	—
(VIII)		50	99 (6)	0.990	1.4670	54.39	54.28	73.62, 73.48	9.54, 9.30	—	74.22	9.27	—

*According to the literature data [7] for substances: (I) b. p. 54-57° (11 mm), (II) 75-77° (13 mm), (III) 92-95° (13 mm); according to [13] for substance (IV) b. p. 83-85° (22 mm).

(continuation)

Substance No.	Formula	Yield (%)	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Analysis data (%) found C	found H	found Cl	calculated C	calculated H	calculated Cl
(IX)		48	127—128 (10)	1.172	1.4980	50.14	49.92	—	—	17.85, 18.20	—	—	17.70
(X)		61	186—187 (17)	1.103	1.5410	64.94	64.53	78.40, 78.39	7.23, 7.19	—	78.94	7.02	—
(XI)		70	154—156 (2)	1.184	1.5212	57.41	57.55	58.96, 58.84	5.99, 5.74	—	59.19	5.83	—

EXPERIMENTAL

The condensation of cyclopentadiene with the various unsaturated compounds proceeded at 160-195° over a period of 7-12 hours. An equimolecular mixture of cyclopentadiene and the other unsaturated compound was sealed in a glass tube and heated in a steel autoclave for 7-12 hours at the given temperature. At the end of the reaction, the reaction mixture was carefully fractionated in vacuum. The compounds obtained and their properties are given in the table.

The reaction of arylacetylenes with cyclopentadiene proceeded under the same conditions. After distilling off the unreacted starting materials and dicyclopentadiene in vacuum, we purified the solid substances obtained by reprecipitation from a suitable solvent and analyzed them.

SUMMARY

The reaction of cyclopentadiene with various esters of allyl alcohol was studied. A series of derivatives of bicyclo-(2,2,1)-heptenyl-5-carbinol-2, that are not described in the literature, were synthesized.

LITERATURE CITED

[1] N. N. Mel'nikov, and L. G. Vol'fson, Chem. Ind. 1953, 413.

[2] L. G. Vol'fson, N. N. Mel'nikov, A. F. Plate, Iu. N. Sapozhkov and G. S. Taits, Proc. Acad. Sci. USSR 105, 1252 (1955).*

[3] U. S. Patent 2519190; Ch. A. 45, 647 (1951).

[4] Brit. Patent 699372; and 699373; Ch. A. 49, 2513 (1955).

[5] U. S. Patent 2635979; Ch. A. 47, 6596 (1953).

[6] S. A. Rohwer, Ch. A. 44, 2690 (1950).

[7] K. Alder and E. Windemuth, Ber. 71, 1939 (1938).

[8] A. F. Plate and T. A. Meerovich, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1947, 219.

[9] N. D. Zelinskii, B. A. Kazanskii and A. F. Plate, J. Gen. Chem. 4, 168 (1934).

[10] A. F. Plate and M. A. Prianishnikova, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1956, 741.*

[11] Belg. Patent 498176; Ch. A. 49, 372 (1955).

[12] E. M. Terent'eva and A. F. Plate, Prog. Chem. 20, 560 (1951).

*Original Russian pagination. See C. B. Translation.

[13] L. Schmerling, J. P. Huvisi and R. W. Welch, J. Am. Chem. Soc. 78, 2819 (1956).

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ORGANIC INSECTOFUNGICIDES

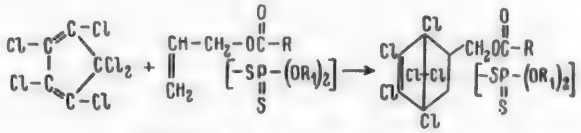
XXIX. THE REACTION OF HEXACHLOROCYCLOPENTADIENE WITH SOME UNSATURATED COMPOUNDS*

S. S. Kukalenko and N. N. Mel'nikov

Although hexachlorocyclopentadiene has a somewhat lower reactivity than cyclopentadiene, as is known, it is still capable of reacting with various unsaturated compounds either of the aliphatic or alicyclic series. Thus, it reacts relatively readily with vinyl chloride, cyclopentadiene, cyclopentene, bicycloheptene, bicycloheptadiene and certain other compounds [1-4]. Many of the compounds prepared by diene synthesis from hexachlorocyclopentadiene have been used practically in agriculture against plant pests and in industry for the manufacture of plastics [5-7]. Of these compounds the major ones are as follows: chlorodan, heptachlorine, aldrin, dieldrin, isodrin and endrin, which are used as insecticides against the most varied harmful insects. Doubtlessly, further study of the hexachlorocyclopentadiene reaction will make it possible to synthesize valuable new compounds which will find use in a wide range of agricultural fields.

In order to find new active insecticides, we studied the reaction products of hexachlorocyclopentadiene with various unsaturated compounds and, first of all, with some esters of allyl alcohol and bicyclo-(2,2,1)-heptenyl-5-carbinol-2. In addition, we studied the reactions of hexachlorocyclopentadiene with ethyl and isobutyl vinyl ethers which M. F. Shostakovskii kindly gave us, and we would like to take this opportunity to thank him.

The allyl esters of various carboxylic acids and dialkylallyl esters of dithiophosphoric acid reacted quite readily with hexachlorocyclopentadiene on heating equimolecular amounts of the starting materials at 100-125° for 10-12 hours and the corresponding adducts were obtained in 50-60% yields. These reactions may be represented by the following general scheme (I).



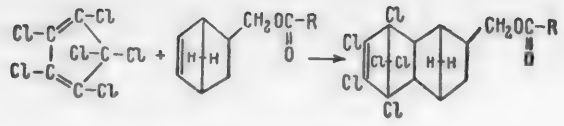
$R = CH_3, C_2H_5, C_3H_7, C_3H_7\text{-iso}, CH_2Cl, C_6H_5$.

$R_1 = C_2H_5$.

The compounds we obtained and their properties are listed in the table. It should be noted that some of the compounds given in the table are described in the literature, but they were either prepared by different methods or no constants were given for them.

Hexachlorocyclopentadiene condensed much more slowly with esters of bicyclo-(2,2,1)-heptenyl-5-carbinol-2 and the reaction mixture had to be heated for not less than 15 hours at 125-130° to obtain a 50% adduct yield. Hexachlorocyclopentadiene reacted with esters of bicyclo-(2,2,1)-heptenyl-5-carbinol-2 by scheme (II).

*From S. S. Kukalenko's Candidate Thesis.



R = CH_3, $C_4H_9CH_3$, C_3H_7, C_3H_7-iso, CH_2Cl, C_6H_5.

The compounds we obtained and their properties are listed in the table.

Of the compounds studied, the vinyl ethers reacted most readily with hexachlorocyclopentadiene as they were added at 80-90° while the bicyclic compounds reacted with hexachlorocyclopentadiene much more slowly and at a higher temperature.

A study of the insecticide properties of the compounds we synthesized showed that they were much less active than aldrin and even chlorindan (1,2,4,5,6,7,8,8-octachloro-4,7-endomethylene-3a,4,7,7a-tetrahydroindan).

EXPERIMENTAL

Condensation of hexachlorocyclopentadiene with allyl esters. For the preparation of the esters of 1,2,3,4,7,7-hexachlorobicyclo-(2,2,1)-heptenyl-2-carbinol-6 equilimolecular mixtures of hexachlorocyclopentadiene and the appropriate allyl ester were heated in sealed tubes at 105-110° for 10-12 hours (excluding only the condensation of hexachlorocyclopentadiene with diethylallyl dithiophosphate, when the condensation was performed at 120-125°). After heating and cooling, the tubes were opened and the reaction products carefully fractionated in vacuum not less than twice and analyzed. We should note that the acetate and propionate of 1,2,3,4,7,7-hexachlorobicyclo-(2,2,1)-heptenyl-2-carbinol-6 were recently described by McBee et al. [8], but they were prepared by other methods. The corresponding butyrate is also described in the literature [9]. The compounds we synthesized and their properties are listed in the table.

Condensation of hexachlorocyclopentadiene with esters of bicyclo-(2,2,1)-heptenyl-2-carbinol-5. An equimolecular mixture of hexachlorocyclopentadiene and bicyclo-(2,2,1)-heptenyl-2-carbinol-5 was heated at 125-130° for 15 hours. After the reaction, the reaction mixture was either fractionated in high vacuum or treated with a small amount of methyl alcohol after cooling. In the latter case, the crystalline product which separated was filtered off and recrystallized from an appropriate solvent. In the case of the benzoate we synthesized, which was a viscous liquid, distillation in high vacuum was accompanied by some decomposition and it was therefore purified by passing a benzene solution through a chromatography column filled with active aluminum oxide. After distilling off the benzene in vacuum, we obtained an analytically pure sample. We should note, however, that this compound and also the others we synthesized, could exist in the form of several stereoisomers, which have not been separated up to now and must be the subject of further investigation.

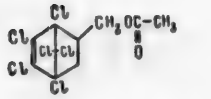
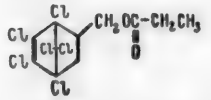
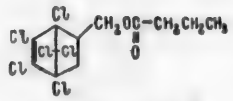
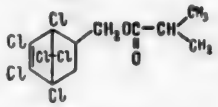
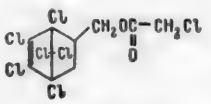
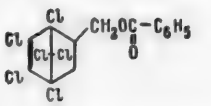
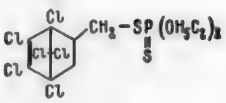
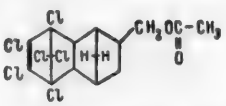
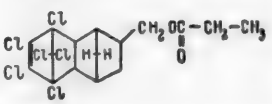
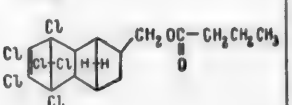
The substances we prepared and their properties are listed in the table.

Condensation of hexachlorocyclopentadiene with vinyl ethers. a) A mixture of 16.4 g of hexachlorocyclopentadiene and 5 g of ethyl vinyl ether was heated in a sealed tube at 80-90° for 6 hours. At the end of the reaction and after cooling, the product obtained was fractionated. As a result of the fractionation we isolated 2 g of unreacted ethyl vinyl ether, 8 g of hexachlorocyclopentadiene and 7.5 g of adduct [1,2,3,4,7,7-hexachloro-5-ethoxybicyclo-(2,2,1)-heptene-2].

B. p. 134-135° (5 mm) d_4^{20} 1.5576, n_D^{20} 1.5358, MR_D 68.98; calc. 69.34.

Found %: C 31.56, 31.48; H 2.43, 2.61; Cl 61.96, 61.47. $C_9H_8OCl_6$. Calculated %: C 31.30; H 2.31; Cl 61.73.

b) A mixture of 5 g of vinyl isobutyl ether and 13.6 g of hexachlorocyclopentadiene was heated in a sealed tube at 110° for 8 hours. At the end of the reaction, the mixture obtained was fractionated in vacuum. We isolated 3 g of vinyl isobutyl ether, 8 g of hexachlorocyclopentadiene and 5 g of 1,2,3,4,7,7-hexachloro-5-isobutoxybicyclo-(2,2,1)-heptene-2.

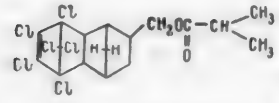
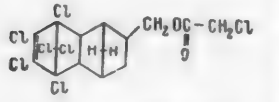
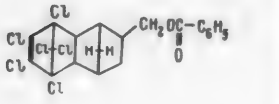
Formula	Boiling point (mm pressure)	Yield (%)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	Cl (%) found	Cl (%) calc.
	178—179° (8.5—9) *	47	1.5630	1.5340	74.13	74.25	57.43, 57.00	57.10
	162—163 (1.5) **	54	1.5280	1.5328	7856	78.77	55.2, 55.12	55.03
	156—157 (0.4) ***	60	1.4850	1.5280	83.58	83.77	53.81, 53.85	53.11
	186—187 (6.5)	49	1.4950	1.5310	8341	83.77	53.56, 53.83	53.11
	173—174 (0.4)	39	1.6500	1.5510	78.79	79.12	61.01, 61.35	60.90
	196—197 (0.4) m.p. 65—66°	31	—	—	—	—	48.77, 49.35	48.96
	—	56	1.4859	1.5660	109.6	110.3	40.31, 40.88	40.41
	185—187 (0.7) m.p. 78—79°	50	—	—	—	—	49.10, 49.07	48.50
	182—183 (0.2)	42	1.4791	1.5498	97.54	97.56	46.82, 47.03	47.02
	198—199 (0.75) m.p. 74—75°	43	—	—	—	—	46.11, 45.89	45.61

• According to the literature data [8]: b. p. 154-155° (2 mm), n_D^{20} 1.533.

•• According to the literature data [8]: b. p. 160-161° (2 mm) n_D^{20} 1.532.

••• According to the literature data [8]: b. p. 158-159° (0.5 mm) n_D^{20} 1.527.

(continuation)

Formula	Boiling point (mm pressure)	Yield (%)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	Cl (%) found	Cl (%) calc.
	186—187° (0.9) m.p. 86—87°	48	—	—	—	—	45.71, 46.07	45.61
	201—202 (0.2) m.p. 70—71°	34	—	—	—	—	52.23, 52.60	52.48
	227—228 (0.4)	48	1.4547	—	—	—	42.51, 42.16	42.59

B. p. 145-146° (4 mm), d_4^{20} 1.4460, n_D^{20} 1.5276, MR_D 79.30; calc. 78.98.

Found %: Cl 57.40, 56.88. $C_{11}H_{12}OCl_6$. Calculated %: Cl 57.11.

SUMMARY

The condensation of hexachlorocyclopentadiene with esters of allyl alcohol and bicyclo-(2,2,1)-heptenyl-2-carbinol-5 and vinyl ethers was studied. It was shown that this reaction gave normal products of diene synthesis, in which hexachlorocyclopentadiene reacted as a diene and the other unsaturated compounds as dienophils. A series of compounds, that have not been described in the literature were synthesized.

LITERATURE CITED

[1] E. T. McBee, J. D. Idol and J. R. and C. W. Roberts, J. Am. Chem. Soc. 77, 6674 (1955).

[2] L. G. Vol'fson, N. N. Mel'nikov, A. F. Plate, Iu. N. Sapozhkov and G. S. Taits, Proc. Acad. Sci. USSR 105, 1252 (1955).*

[3] Belg. Patent 498176; Ch. A. 49, 372 (1955).

[4] U. S. Patent 2676131 and 2676132 (1954); Ch. A. 48, 8473 (1954).

[5] N. N. Mel'nikov and L. G. Vol'fson, Chem. Ind. 1953, 413.

[6] Brit. Patent 698213; Ch. A. 49, 2512 (1955).

[7] P. Robitschek and Thomas Bean, Ind. Eng. Ch. 46, 1628 (1954).

[8] E. T. McBee and Rakoff, J. Am. Chem. Soc. 77, 4427 (1955).

[9] Ellis K. Fields, J. Am. Chem. Soc. 76, 2709 (1954).

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TERTIARY AMINES OF SOME HETEROCYCLICS AS POSSIBLE HYPOTENSION REMEDIES

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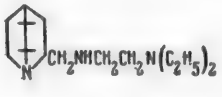
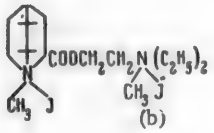
Until recently, in searching for ganglioblocking media, special attention was paid to quaternary ammonia salts as among them are compounds which are used practically in medicine [1]. It was considered that the ganglioblocking effect was due to the quaternary nitrogen. However, factual material that has collected shows that compounds with a similar effect are also found among certain tertiary and secondary amines. In 1950 M. D. Mashkovsky et al., made the first observations of this nature [2]. Later, analogous data appeared in the foreign literature [3].

A recent study of quinuclidine derivatives [4], that we synthesized, showed the very high ganglioblocking activity of a series of compounds that were secondary-tertiary amines. Thus, for example, 2-diethylaminoethylaminomethylquinuclidine (a) has a high ganglioblocking effect similiar to that of the dimethiodide of the diethylaminoethyl ester of α-quinuclidinecarboxylic acid (b), described previously [1].

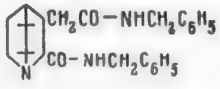


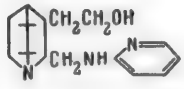
(a)



(b)

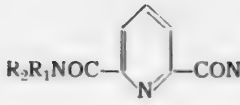
Other substituted quinuclidines, which are secondary-tertiary amines, such as the dibenzylamide of [2-carboxyquinuclidyl-(3)]-acetic acid [5] and 2-[(pyridyl-2')-aminomethyl]-3-(β-hydroxyethyl)-quinuclidine [6] were also found to be highly active.





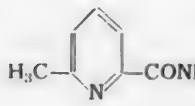
As compounds with a ganglioblocking effect have a definite value in hypertonia therapy, it seemed advantageous to continue the investigations in order to find simpler compounds. The preparation of analogous amines of the pyridine and piperidine series was especially interesting as our previous investigation showed that the substitution of a piperidine for a quinuclidine ring hardly affected the character and activity of this type of preparation. For this reason we synthesized a series of compounds of the pyridine and piperidine series.

The starting substances were dipicolinic and 6-methylpicolinic acids, prepared by oxidizing 2,6-lutidine, which is a waste product in phthivazide production. The chlorides or esters of these acids reacted with various amines to give the corresponding amides (I and II).



(I)

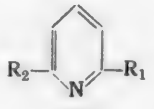
(a) $R_1 = R_2 = CH_3$; (b) $R_1 = R_2 = C_2H_5$;
(c) $R_1 = H$; $R_2 = CH_2CH_2N(C_2H_5)_2$;
(d) $R_1 = H$; $R_2 = CH(CH_3)(CH_2)_3N(C_2H_5)_2$;
(e) $R_1 = H$; $R_2 = CH_2C_6H_5$;
(f) $R_1 = H$; $R_2 = \alpha$-pyridyl



(II)

(a) $R = H$; $R_2 = CH_2CH_2N(C_2H_5)_2$;
(b) $R = H$; $R_2 = CH_2C_6H_5$;
(c) $R = H$; $R_2 = A$-pyridyl

Contrary to literature reports that amines cannot be prepared from pyridinecarboxylic amides using lithium aluminum hydride, we were able to convert most of the amides obtained into amines (III).

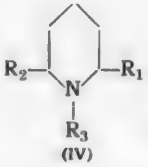


(III)

(a) $R_1 = R_2 = CH_2N(C_2H_5)_2$;
(b) $R_1 = R_2 = CH_2NHCH_2C_6H_5$;
(c) $R_1 = R_2 = CH_2NH(\alpha\text{-}C_5H_4N)$;
(d) $R_1 = CH_3$; $R_2 = CH_2NHCH_2C_6H_5$;
(e) $R_1 = CH_3$; $R_2 = CH_2NH(\alpha\text{-}C_5H_4N)$.

However, the reaction proceeded with the formation of side products and gave, as a rule, low amine yields.

The piperidinecarboxylic amides could be reduced much better. In this case good yields of amines were obtained and they could be isolated without difficulty. This made it possible to prepare the corresponding amino derivatives of the piperidine series (IV).



(IV)

(a) $R_1 = R_2 = CH_2N(C_2H_5)_2$; $R_3 = H$;
(b) $R_1 = R_2 = CH_2N(C_2H_5)_2$; $R_3 = CH_3$;
(c) $R_1 = CH_2NHCH_2C_6H_5$; $R_2 = CH_3$; $R_3 = H$;
(d) $R_1 = CH_2-N(CH_3)-CH_2C_6H_5$; $R_2 = R_3 = CH_3$;
(e) $R_1 = CH_2NHCH_2CH_2N(C_2H_5)_2$; $R_2 = R_3 = CH_3$.

A pharmacological study, carried out by I. M. Sharapov in a pharmacological laboratory, on the pyridine and piperidine derivatives showed that 1,6-dimethyl-2-(β-diethylaminoethylaminomethyl)-piperidine (IV e) had a high ganglioblocking activity, 10 times greater than the tetraethylammonium iodide. The rest of the compounds had no value as ganglioblocking agents.

EXPERIMENTAL

Di-(dimethylamide) of dipicolinic acid. The diacid chloride, prepared from 3 g of dipicolinic acid [1], was gradually added to 120 ml of a 14.5% solution of dimethylamine in absolute ether. The reaction mixture was stirred for 8 hours at room temperature, then excess of a 50% solution of potassium carbonate was added and the solution extracted with ether. The ether extract was dried over baked potassium carbonate and the ether distilled off. We obtained 1.3 g (32%) of a white crystalline substance, which was soluble in the usual organic solvents and in water. The m. p. was 144-146°.

Found %: C 59.92; H 6.76; N 19.25. $C_{11}H_{15}O_2N_3$. Calculated %: C 59.71; H 6.83; N 18.99.

Di-(diethylamide) of dipicolinic acid. The diacid chloride, prepared from 3 g of dipicolinic acid was added to a solution of 26 g of diethylamine in 100 ml of absolute ether. The reaction mixture was treated as described above. We obtained 4.16 g (85%) of a substance with b. p. 170-172° (0.25 mm). The substance was soluble in the usual organic solvents and in water. On standing, the substance crystallized. The m. p. was 74.5-76.5° (from petroleum ether).

Found %: C 64.60; H 8.26; N 14.96. $C_{15}H_{23}O_2N_3$. Calculated %: C 64.95; H 8.35; N 15.22.

2,6-Di-(diethylaminomethyl)-pyridine. Three g of the di-(diethylamide) of dipicolinic acid was reduced for 20 hours with 1.23 g of lithium aluminum hydride in 100 ml of absolute ether under the conditions described previously [4]. We obtained 1.75 g (65%) of a straw-yellow, oily substance with b. p. 100-102° (0.35 mm). The substance was soluble in the usual organic solvents and in water.

Found %: C 72.41; H 10.79. $C_{15}H_{27}N_3$. Calculated %: C 72.23; H 10.91.

Di-(diethylamide) of dipipecolinic acid. 8.7 g of the di-(diethylamide) of dipicolinic acid was dissolved in 100 ml of anhydrous ethyl alcohol, 8 ml of a 15% alcohol solution of hydrogen chloride added and the solution hydrogenated at room temperature in the presence of 0.4 g of platinum oxide at a pressure of 40-60 cm of water. The hydrogenation was complete in 6 hours. The catalyst was filtered off and the filtrate evaporated to dryness in vacuum. The residue was treated with excess of a 50% potassium carbonate solution and extracted with ether. The ether extract was dried with baked potassium carbonate, the ether distilled off and the residue vacuum distilled. We obtained 7.5 g (84%) of an oily, colorless liquid with b. p. 175-177° (0.3 mm). The substance was soluble in the usual organic solvents and in water.

Found %: C 63.46; H 10.37; N 15.02. $C_{15}H_{29}O_2N_3$. Calculated %: C 63.56; H 10.31; N 14.82.

2,6-Di-(diethylaminomethyl)-piperidine. 3.5 g of di-(diethylamide) of dipipecolinic acid was reduced for 20 hours with 1.4 g of lithium aluminum hydride in 100 ml of absolute ether. We obtained 2.3 g (73%) of a yellowish liquid, which was soluble in the usual organic solvents and in water. The b. p. was 105° (0.5 mm).

Found %: C 70.70; H 12.74; N 16.17. $C_{15}H_{33}N_3$. Calculated %: C 70.52; H 13.02; N 16.45.

N-Methyl-2,6-di-(diethylaminomethyl)-piperidine. 2.2 g of 2,6-di-(diethylaminomethyl)-piperidine was heated on a boiling water bath for 15 hours with 0.83 g of 33.5% formalin, 1.49 g of formic acid and 1.32 ml of water. The reaction mixture was treated with excess of a 50% solution of potassium carbonate and extracted with ether. After drying the extract and distilling off the ether, we vacuum distilled the residue. We obtained 1.73 g (74%) of a colorless, mobile liquid with b. p. 84-86° (0.2 mm).

Found %: N 15.63, 15.72. $C_{16}H_{35}N_3$. Calculated %: N 15.59.

Di-(diethylaminoethylamide) of dipicolinic acid. From the diacid chloride, prepared from 6 g of dipicolinic acid, and using the method described for the synthesis of the di-(diethylamide) of dipicolinic acid, we prepared 9.38 g (72%) of a caramel-like, light yellow substance with b. p. 223-225° (0.6 mm), which was soluble in the usual organic solvents and in water.

Found %: C 62.38; H 8.96; N 19.31. $C_{19}H_{33}O_2N_5$. Calculated %: C 62.78; H 9.15; N 19.26.

Di-(diethylaminoisopentylamide) of dipicolinic acid. The diacid chloride, prepared from 3 g of dipicolinic acid, was treated as described above with 11.3 g of diethylaminoisopentylamine, dissolved in 100 ml of absolute ether. The yield was 5.6 g (70%). The b. p. was 225-227° (0.35 mm). The substance was soluble in the usual organic solvents and in water.

Found %: C 67.04; H 10.07. $C_{25}H_{45}O_2N_5$. Calculated %: C 67.07; H 10.37.

The dimethiodide was a white, hygroscopic substance with m. p. 125°.

Found %: N 9.22, 9.25; I 34.24. $C_{27}H_{51}O_2N_5I_2$. Calculated %: N 9.52; I 34.69.

The dibenzylamide of dipicolinic acid. 7.7 g of benzylamine, dissolved in 100 ml of absolute ether, was added to the diacid chloride dipicolinic acid prepared from 4 g of the acid. At the end of the reaction, the precipitate formed was filtered off, carefully washed with chloroform and the chloroform extract shaken

twice with 25 ml of a 50% potassium carbonate solution, dried with baked potassium carbonate and the chloroform distilled off in vacuum. The solid residue was recrystallized from alcohol. We obtained 4.36 g (53%) of a substance, which was soluble in chloroform and hot water, difficultly soluble in ether and insoluble in water. The m. p. was 179-181°.

Found %: C 72.90; H 5.50; N 12.03, 12.08. $C_{21}H_{19}O_2N_3$. Calculated %: C 73.02; H 5.54; N 12.16.

2,6-Di-(benzylaminomethyl)-pyridine. 6.45 g of the dibenzylamide of dipicolinic acid was reduced for 20 hours with 2.13 g of lithium aluminum hydride in 120 ml of a mixture of absolute ether and benzene (1:1). We obtained 0.6 g (10%) of a light yellow, oily substance with b. p. 207° (0.5 mm), which was soluble in the usual organic solvents and insoluble in water. The bulk of the products (2-2.5 g) became tarry on distillation.

Found %: N 13.04, 13.26. $C_{21}H_{23}N_3$. Calculated %: N 13.23.

Di-(pyridyl-2)-amide of dipicolinic acid. 11.2 g of α-aminopyridine was added to the diacid chloride, prepared from 4 g of dipicolinic acid, dissolved in 50 ml of anhydrous benzene. The reaction mixture was heated for 3 hours at 60° and then cooled and the crystals formed filtered off, ground in a mortar with 25 ml of water, again filtered and washed with alcohol and ether. We obtained 4.3 g (56%) of colorless)crystals as small needles. The substance was insoluble in water, difficultly soluble in alcohol and ether and soluble in hot pyridine. The m. p. was 225-226°.

Found %: N 22.12, 21.87. $C_{17}H_{13}O_2N_5$. Calculated %: N 21.93.

2,6-Di-(pyridyl-2')-aminomethylpyridine. 3.1 g of the di-(dipyridyl-2')-amide of dipicolinic acid was reduced for 20 hours with 1.14 g of lithium aluminum hydride in 75 ml of a mixture of ether and toluene (1:2). We obtained 0.2 g (7%) of a substance with m. p. 147-149°, which was soluble in toluene, benzene and ethyl alcohol. 1.5 g of the starting diamide was isolated by extracting the precipitate of lithium and aluminum hydroxides with pyridine.

Found %: C 69.65; H 5.73; N 24.12, 24.28. $C_{17}H_{17}N_5$. Calculated %: C 70.07; H 5.88; N 24.05.

Diethylaminoethylamide of 6-methylpicolinic acid. The reaction was performed as in the case of the corresponding amide of dipicolinic acid. From the acid chloride, prepared from 4 g of 6-methylpicolinic acid, and 10 g of diethylaminoethylamine, dissolved in 100 ml of absolute ether, we obtained 4.4 g (64%) of a colorless, oily substance with b. p. 149-152° (0.5 mm), which was soluble in the usual organic solvents.

Found %: N 17.71, 18.08. $C_{13}H_{21}ON_3$. Calculated %: N 17.86.

Benzylamide of 6-methylpicolinic acid. The benzylamide of 6-methylpicolinic acid was synthesized by two methods.

a) The acid chloride, prepared from 3 g of 6-methylpicolinic acid, was treated with 7 g of benzylamine, dissolved in 100 ml of absolute ether. We obtained 2.15 g (43%) of a substance with b. p. 189-191° (0.4 mm). The white crystals were difficultly soluble in alcohol and ether and insoluble in water. The m. p. was 96-98°.

Found %: C 74.15, 74.32; H 6.23, 6.33; N 12.46. $C_{14}H_{14}ON_2$. Calculated %: C 74.30; H 6.23; N 12.38.

b) A mixture of 4 g of ethyl 6-methylpicolinate and 20 g of benzylamine was boiled for 48 hours. The yield was 2,94 g (54%). The m. p. was 96-98°. A mixture of the substance with the benzylamide, prepared via the acid chloride, did not show depression of melting point.

2-Methyl-6-benzylaminomethylpyridine. 2.95 g of the benzylamide of 6-methylpicolinic acid was reduced for 20 hours with 0.74 g of lithium aluminum hydride in 165 ml of absolute ether. We obtained 0.65 g of a substance (23%) with b. p. 119° (0.1 mm). The substance was soluble in organic solvents and insoluble in water.

Found %: N 13.05, 13.18. $C_{14}H_{16}N_2$. Calculated %: N 13.19.

Benzylamide of 6-methylpipecolinic acid. Five g of ethyl 6-methylpipecolinate [1] was boiled with 25 ml of freshly distilled benzylamine. The yield was 4.6 g (65%). The colorless, oily liquid, with low mobility, was readily soluble in the usual organic solvents and insoluble in water. The b. p. was 164-166° (0.35 mm).

Found %: C 72.34, 72.18; H 8.40, 8.50. $C_{14}H_{20}ON_2$. Calculated %: C 72.37; H 8.67.

2-Methyl-6-benzylaminomethylpiperidine. Three g of the benzylamide of 6-methylpipecolinic acid was reduced for 40 hours with 0.61 g of lithium aluminum hydride in 110 ml of a mixture of ether and benzene (1:1). We obtained 2.05 g (73%) of an oily, straw yellow substance, which was soluble in the usual organic solvents and insoluble in water. The b. p. was 121-122° (0.1 mm).

Found %: C 76.81; H 9.82; N 12.48. $C_{14}H_{22}N_2$. Calculated %: C 77.00; H 10.15; N 12.85.

1,6-Dimethyl-2-benzylmethylaminomethylpiperidine. A mixture of 1.85 g of 2-methyl-6-benzylaminomethylpiperidine, 2.6 ml of water, 1.64 g of 33.5% formalin solution and 2.92 g of formic acid was heated for 15 hours on a boiling water bath. The cooled solution was treated with excess of 50% potassium carbonate and extracted with ether. After drying the ether extract and distilling off the solvent we distilled the residue. We obtained 1.46 g (69.8%) of a colorless, oily substance with b. p. 128-130° (0.25 mm). The substance was soluble in the usual organic solvents and insoluble in water.

Found %: C 78.00, 77.95; H 10.19, 10.32; N 11.28, 11.25. $C_{16}H_{26}N_2$. Calculated %: C 77.99; H 10.63; N 11.37.

(Pyridyl-2')-amide of 6-methylpicolinic acid. Four g of the ester of 6-methylpicolinic acid and 20 g of α-aminopyridine were heated for 40 hours at 180° (in the bath). After this the mass was dissolved in water, the heavy, insoluble brown oil separated off in a separating funnel, dissolved in ether, dried with sodium sulfate and distilled after evaporation of the solvent. We obtained 2.44 g (47%) of a substance with b. p. 153° (0.35 mm), which was readily soluble in the usual organic solvents and insoluble in water.

Found %: C 67.47; H 5.31; N 19.79. $C_{12}H_{11}ON_3$. Calculated %: C 67.64; H 5.20; N 19.70.

2-Methyl-6-(piperidyl-2')-aminomethylpyridine. 2.12 g of the (pyridyl-2')-amide of 6-methylpicolinic acid was reduced for 20 hours with 0.56 g of lithium aluminum hydride in 55 ml of absolute ether. We obtained 0.70 g (35%) of a substance, which was soluble in the usual organic solvents and in water.

Found %: N 71.95; H 7.55; C 21.24. $C_{12}H_{13}N_3$. Calculated %: C 72.33; H 6.57; N 21.09.

Diethylaminoethylamide of 1,6-dimethylpipecolinic acid. 5 g of ethyl 1,6-dimethylpipecolinate [1] and 17.5 g of diethylaminoethylamine was heated for 40 hours so that the mixture boiled gently. The excess diethylaminoethylamine was distilled off and the residue vacuum distilled. We obtained 4.03 g (58%) of a light yellow, oily substance with b. p. 165-167° (6 mm).

Found %: N 16.63, 16.78. $C_{14}H_{29}ON_3$. Calculated %: N 16.45.

1,6-Dimethyl-2-(diethylaminoethylaminomethyl)-piperidine. Four g of the diethylaminoethylamide of 1,6-dimethylpipecolinic acid was reduced for 20 hours with 1.26 g of lithium aluminum hydride in 80 ml of absolute ether. We obtained 2.8 g (74%) of a substance with b. p. 125-127° (5 mm), which was soluble in the usual organic solvents and in water.

Found %: N 17.27, 17.66. $C_{14}H_{31}N_3$. Calculated %: N 17.40.

SUMMARY

1. Starting with lutidine, a series of substituted pyridine and piperidine amides and amines were synthesized.

2. In contrast to piperidinecarboxylic amides, pyridinecarboxylic amides were difficult to reduce with lithium aluminum hydride to the corresponding amines.

3. Pharmacological investigation showed that of the substances synthesized, only 1,6-dimethyl-2-(diethylaminoethylaminomethyl)-piperidine had a high ganglioblocking activity.

LITERATURE CITED

[1] M. V. Rubtsov, E. S. Nikitskaia and V. S. Usovskaia, J. Gen. Chem. 26, 130 (1956).*

[2] M. D. Mashkovskii, Pharmacol. and Toxicol. 13, 42 (1950); Iu. I. Syrneva, Pharmacol. and Toxicol. 13, 26 (1950); M. D. Mashkovskii and L. E. Rabkina, Pharmacol. and Toxicol. 15, 23 (1952); P. M. Dozortseva, Pharmacol. and Toxicol. 18, 17 (1955).

[3] A. J. Plummer, J. A. Scheider and W. E. Barrett, Arch. int. pharmacodyn. 98, 1 (1954); A. P. Phillips, J. Am. Chem. Soc. 76, 2211 (1954); R. V. Ford, J. C. Madison and J. H. Moyer, Amer. j. med. Sciences, 232, 129 (1956).

[4] M. V. Rubtsov and E. S. Nikitskaia, J. Gen. Chem. 24, 1659 (1954).*

[5] M. V. Rubtsov, E. S. Nikitskaia, E. E. Mikhlina, A. D. Ianina and V. Ia. Furshtatova, J. Gen. Chem. 23, 1955 (1953).*

[6] M. V. Rubtsov, E. E. Mikhlina and V. Ia. Furshtatova, J. Gen. Chem. 24, 2217 (1954).*

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SYNTHESIS OF RACEMIC METHYL ETHER OF O,O-DIBENZYLMAGNOLINE

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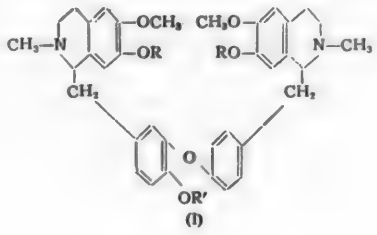
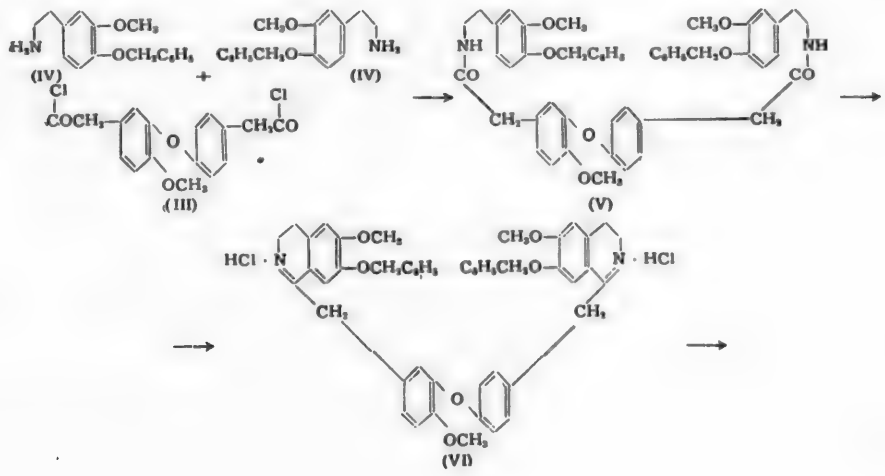
The alkaloid magnoline (I, R = R' = H) was isolated together with magnolamine by N. F. Proskurnina and A. P. Orekhov [1] in 1938 from the leaves of the Caucasian magnolia (Magnolia fusata of the family Magnoliaceae). The structure of magnoline was established by the oxidative decomposition of its trimethyl ether [2] (I, R = R' = CH_3). Here the following compounds were isolated: 1-oxo-6,7-dimethoxy-2-methyl-tetrahydroisoquinoline and 2- methoxy-4',5-dicarboxydiphenyl ether. The position of the free hydroxyl groups was established by the oxidation of the triethyl ether of the alkaloid. On the basis of the performed studies the following formula was proposed for magnoline (I, R = R' = H).

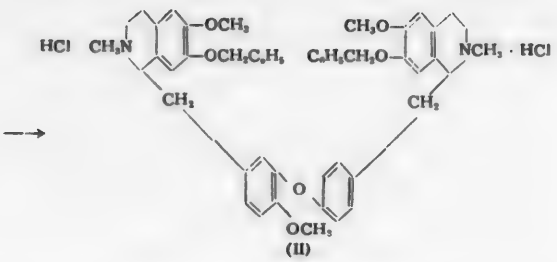


(I)

We synthesized the dihydrochloride of 2-methoxy-4',5-bis-(6-methoxy-7-benzyloxy-2-methyl-1,2,3,4-tetrahydro-1-isoquinolylmethyl)-diphenyl ether (II), which after removal of the benzyl radicals can be converted into the (±) methyl ether of magnoline (I, R = H, R' = CH_3).



(VII)



(II)

The starting compounds for the synthesis were the dichloride of 2-methoxy-4',5-bis(carboxymethyl)diphenyl ether [3] (III) and 3-methoxy-4-benzyloxyphenethylamine (IV), which when reacted with each other in the presence of potash gave diamide (V). The latter when reacted with phosphorus pentachloride was converted to the bisdihydroisoquinoline derivative (VI), which was then subjected to catalytic hydrogenation, followed by methylation with formalin in the presence of formic acid.

EXPERIMENTAL

Bis(3-methoxy-4-benzyloxyphenethylamide) of 2-methoxy-4',5-bis(carboxymethyl)diphenyl ether (V). A mixture of 1.3 g of 2-methoxy-4',5-bis(carboxymethyl)diphenyl ether and 4.86 g of thionyl chloride was heated at 50-60° for 2 hours. The excess thionyl chloride was vacuum-distilled, and the residue was dissolved in 30 ml of chloroform. The latter was then gradually added with stirring to a solution of 3-methoxy-4-benzyloxyphenethylamine (isolated from 3.61 g of the hydrochloride) in 50 ml of chloroform. At the same time, maintaining a weakly alkaline medium (phenolphthalein), 6-8 ml of a 10% aqueous solution of potassium carbonate was added. The stirring was continued for another 30 minutes. Then the chloroform layer was separated, washed with 5% hydrochloric acid solution, then with water until neutral, and dried over sodium sulfate. After removal of the solvent in vacuo (15-20 mm) the residue, a brown tarry mass, was rubbed in ether. Here a powder with m. p. 94-96° was obtained. Yield 2.64 g (80.8%). Three recrystallizations from ethyl alcohol gave colorless crystals with m. p. 109-110°.

Found %: C 73.88, 74.12; H 6.65, 6.57; N 3.80, 3.53. $C_{48}H_{50}O_8N_2$. Calculated %: C 74.03; H 6.35; N 3.52.

2-Methoxy-4',5-bis(6-methoxy-7-benzyloxy-3,4-dihydro-1-isoquinolylmethyl)diphenyl ether dihydrochloride (VI). To a solution of 1.3 g of the bis(3-methoxy-4-benzyloxyphenethylamide) of 2-methoxy-4',5-bis(carboxymethyl)diphenyl ether (V) in 8 ml of chloroform was added in drops, with stirring and cooling, a solution of 1.49 g of phosphorus pentachloride in 36 ml of chloroform. The reaction mass was allowed to stand at room temperature for three days, and finally it was heated at the boil for 1 hour. Then it was washed with 2% sodium hydroxide solution, treated with dilute hydrochloric acid, washed with water until neutral (to Congo) and dried over sodium sulfate. After removal of the chloroform in vacuo (15-20 mm) the residue was rubbed in ether. Here a yellow powder was obtained. Precipitation from solution in 25 ml of ethyl alcohol with anhydrous ether gave 0.7 g (51.3%) of product with m. p. 147-153°.

Found %: C 70.86, 70.50; H 5.59, 5.65; N 3.71, 3.43. $C_{48}H_{48}O_6N_2 \cdot 2HCl$. Calculated %: C 70.75; H 5.82; N 3.37.

The dipicrolonate was obtained by the precipitation of the dihydrochloride of the base in chloroform solution with picrolonic acid. Yellow crystals from alcohol. M. p. 167.5-168°.

Found %: C 64.06, 64.12; H 5.18, 4.98; N 10.64, 10.79. $C_{69}H_{62}O_{16}N_{10}$. Calculated %: C 64.38; H 4.86; N 10.90.

2-Methoxy-4',5-bis(6-methoxy-7-benzyloxy-2-methyl-1,2,3,4-tetrahydro-1-isoquinolylmethyl)diphenyl ether dihydrochloride (II). A solution of 0.22 g of the dihydrochloride of 2-methoxy-4',5-bis(6-methoxy-7-benzyloxy-3,4-dihydro-1-isoquinolylmethyl)diphenyl ether (VI) in 20 ml of anhydrous ethyl alcohol was filtered and then hydrogenated over platinum catalyst (from 0.3 g of platinum oxide) with constant shaking for 5 hours at room temperature. The catalyst was removed, while the alcohol was vacuum-distilled (15-20 mm) in a stream of nitrogen. The residue was dissolved in 40 ml of chloroform, shaken with 10% sodium carbonate solution, washed with water until neutral (phenolphthalein), and the solvent removed by vacuum-distillation (15-20 mm). To the residue was added 0.06 ml of 38.4% formalin and 0.17 ml of 88% formic acid, and the whole heated for 5 hours on the water bath. Then 15-20 ml of benzene was added, and 5% sodium hydroxide solution until alkaline. The substance was extracted from the water layer with benzene; the combined extracts were washed with water and dried over sodium sulfate. After filtration, the solution was treated with benzene, saturated with hydrogen chloride. The nearly colorless precipitate was washed by decantation with ether until neutral (to Congo) and then dried. Yield 0.083 g (35%).

Found %: C 68.76; H 6.75; N 3.12. $C_{51}H_{54}N_2O_6 \cdot 2HCl \cdot 1\,{}^1/_2H_2O$. Calculated %: C 68.75; H 6.68; N 3.14.

Nearly colorless crystals were obtained after drying in vacuo (3 mm) for 2 hours at 60°. M. p. 136-138°.

Found %: C 70.76, 70.72; H 6.37, 6.36; N 3.15. $C_{51}H_{54}N_2O_6 \cdot 2HCl$. Calculated %: C 70.90; H 6.53; N 3.24.

SUMMARY

The racemic methyl ether of O,O-dibenzylmagnoline was synthesized.

LITERATURE CITED

[1] N. F. Proskurnina and A. P. Orekhov, J. Gen. Chem. 9, 126 (1939).

[2] N. F. Proskurnina and A. P. Orekhov, J. Gen. Chem. 10, 707 (1940).

[3] I. N. Gorbacheva, G. V. Bushbek, L. P. Varnakova, L. M. Shulov and N. A. Preobrazhenskii, J. Gen. Chem. 27, 2297 (1957).*

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DIENE HYDROCARBONS FROM UNSATURATED ALCOHOLS

I. CATALYTIC DEHYDRATION OF CROTYL ALCOHOL TO BUTADIENE

Iu. A. Gorin, V. S. Ivanov, E. S. Bogdanova and E. A. Piaivinen

Diene hydrocarbons with a conjugated system of double bonds can be obtained by the catalytic dehydration of α, β-unsaturated alcohols. The dehydration of crotyl alcohol yields butadiene. As catalysts for the dehydration of crotyl alcohol various authors used toluidine bisulfate, anhydrous oxalic acid, $KHSO_4$, H_3PO_4, $AlCl_3$ [1], kaolin, $AlPO_4$ [2], precipitated Al_2O_3, [3], and the mixed catalysts kaolin–H_3PO_4 and kaolin–Fe_2O_3–KOH [4]. The yields of butadiene using the indicated catalysts ranged from 25 to 57 mole %, based on passed (taken) alcohol. Iu. A. Gorin [5] investigated the transformations of crotyl alcohol on one of the dehydrating components of the S. V. Lebedev catalyst. The highest yield of butadiene was obtained at 325° (54.2 mole %, based on passed alcohol). According to the studies of the American authors [6], the yield of butadiene from crotyl alcohol over silica gel can reach 75% at 350°. To explain the formation of butadiene from ethyl alcohol by the S. V. Lebedev method, Iu. A. Gorin [7] proposed a scheme in which crotyl alcohol was regarded as being an unstable intermediate product, the dehydration of which gave butadiene. Since the yield of butadiene from ethyl alcohol is very high by the S. V. Lebedev method, then it is obvious that the intermediate stage in its formation–the dehydration of crotyl alcohol–should also proceed with high yield.

In the present investigation we studied the dehydration of crotyl alcohol under conditions close to those of the S. V. Lebedev process. For this we used the various dehydrating components of the S. V. Lebedev catalyst, which made it possible to mold the process to some degree in its last stage–the formation of butadiene by the dehydration of crotyl alcohol. In addition, a study of the transformations of crotyl alcohol over certain dehydrating catalysts under various conditions had as one of its problems the selection of the most effective contacts for the dehydration of crotyl alcohol with the purpose of obtaining butadiene from it in high yield. It seemed of interest to first make a thermodynamical calculation of the reaction for the dehydration of crotyl alcohol in order to determine if its accomplishment was practically feasible. Data on the free energy, heat content, entropy and change in the heat capacity as a function of the temperature are absent for crotyl alcohol. For this reason we limited ourselves to an approximate calculation, using the method based on the additivity of thermodynamic functions for organic molecules.

The reaction is run at temperatures above the boiling point of crotyl alcohol (i.e., above 120°), and consequently proceeds in the gas phase ($\Delta\nu = 1$). Using the data of Bremner and Thomas [8] for the values of the normal free energies of alcohol groups, calculated for a number of temperatures, we calculated the free energy of crotyl alcohol at 300, 600 and 800°K (Table 1). Calculated in this manner, the free energy of formation of crotyl alcohol at 300°K ($\Delta F = -16{,}000$ cal/mole) is found to be in agreement with the results obtained by us using other calculation methods, also based on the property of additivity: $\Delta F_s = -15{,}000$ cal/mole [9], and $\Delta F_s = -16{,}610$ and $-16{,}760$ cal/mole [10]. When the calculation is made starting from liquid primary n-butyl alcohol with its conversion to a gas, followed by dehydration, the value obtained for $\Delta F_s = -16{,}575$ kcal/mole.

Calculation of the change in the free energy of the dehydration reaction makes it possible to determine the equilibrium constants K_p and the yields of butadiene. The values of the free energies for crotyl alcohol, butadiene, water and the reaction for the dehydration of crotyl alcohol, the equilibrium constants K_p, and the yields of butadiene, calculated for 300, 600 and 800°K, are given in Table 1, from which it can be seen that even at 27° (300°K) it is theoretically possible for the reaction to go nearly to completion. The yield increases as the temperature is increased.

TABLE 1

Approximate Thermodynamic Calculation of the Reaction for the Dehydration of Crotyl Alcohol

T (°K)	ΔF (kcal/mole)			Free energies (kcal/mole)	K_p	Yield C_4H_6 (mole %)
	crotyl alcohol	butadiene [11]	water [11]			
300	—16.00	36.49	—54.62	—2.13	36	97.1
600	+7.00	47.21	—51.16	—10.95	9816	~100
800	22.50	54.92	—48.65	—16.23	27350	~100

It should be mentioned that thermodynamic considerations alone cannot serve as a criterion in investigating a chemical reaction. Thermodynamic data should be regarded in association with the chemical peculiarities of the process. In the present case the use of vacuum facilitates a more complete conversion of crotyl alcohol into butadiene, while raising the temperature facilitates this only up to a certain limit, after which the yields of butadiene will decrease due to intensification of secondary processes.

In the present study on the dehydration of crotyl alcohol we investigated the following catalysts: 1) the various dehydrating components of the S. V. Lebedev catalyst—B, B_1, B_2, B_3 and B_4; 2) a complex phosphate catalyst, used by the synthetic rubber industry in Germany for the dehydration of 1,3-butylene glycol to butadiene [12]—F; 3) a calcium phosphate catalyst having the composition: 70% $Ca_3(PO_4)_2$ + 30% $CaHPO_4$ — F_{Ca}; 4) anhydrous magnesium sulfate, the use of which for the dehydration of some α, β-unsaturated alcohols is indicated by D. V. Tishchenko [13], — $MgSO_4$; 5) magnesium sulfate, deposited on silica gel—$MgSO_4$-2; 6) activated aluminum oxide—AOA; 7) silica gel—SiO_2; and 8) silica gel-tantalum catalyst, used in U.S.A. for the preparation of butadiene from a mixture of ethyl alcohol and acetaldehyde—98% SiO_2 + Ta_2O_5 [14].

The results obtained by us in the dehydration of crotyl alcohol over the various catalysts are summarized in Tables 2 and 3.

The results of the experiments on the converison of crotyl alcohol over the various dehydrating components of the S. V. Lebedev catalyst and over some of the phosphate catalysts are given in Table 2.

From the data in Table 2 it follows that using component B makes it possible to obtain substantial yields of butadiene from crotyl alcohol, reaching values as high as 88.5 mole %, based on alcohol passed through. The use of catalyst B_2 creates conditions similar to those that prevail in the process for the preparation of butadiene from ethyl alcohol, where crotyl alcohol is the intermediate product. The fact that butadiene is formed in such high yield in this case indicates that the intermediate stage of the formation and dehydration of crotyl alcohol does not serve to impede progress of the S. V. Lebedev process. Liquid products were obtained together with butadiene when catalyst B_2 was used, which were found to contain methylvinylcarbinol, formed as the result of allylic rearrangement of the crotyl alcohol. For catalysts of the B type the optimum temperature for the decomposition of crotyl alcohol proved to be 350°.

The gaseous products obtained when the complex phosphate catalyst F was used were found to contain nearly pure butadiene, the yield of the latter reaching 82 mole %. The gas from the experiments with calcium phosphate was also rich in butadiene, but the yields of the latter were lower.

The experimental data on the dehydration of crotyl alcohol over magnesium sulfate, activated aluminum oxide, and silica gel in a mixture of silica gel with tantalum pentoxide, are presented in Table 3. The maximum yields of butadiene were obtained using magnesium sulfate deposited on silica gel ($MgSO_4$-2). The use of activated aluminum oxide gave a much lower yield of butadiene than that obtained with the other catalysts. Here the process for the dehydration of crotyl alcohol is complicated by side reactions, as evidenced by the greater amount of butylenes in the gas (up to 34 volume %). The formation of butylenes can be explained by stating that crotyl alcohol under the influence of aluminum oxide is partially isomerized to butyraldehyde, which is then reduced by the crotyl alcohol to butyl alcohol. The dehydration of the latter yields butylenes.

TABLE 2

Catalytic Dehydration of Crotyl Alcohol Over Various Dehydrating Components of the S. V. Lebedev Catalyst and Over Phosphate Catalysts

Expt. No.	Catalyst	Expt. temp., (°C)	Admittance (ml/hr/ml catalyst)	Diluent and degree of dilution (mole)	Alcohol passed (g)	Air-free gas (l stand. conditions)	Composition of gas (volume %)						C_4H_6 on alcohol passed (mole %)
							CO_2	$C_4H_8+C_3H_6$	C_2H_4	CO	H_2	CH_4	C_4H_6	
1	B	325°	0.69	—	4.25	0.87	2.9	11.7	0.6	0.0	0.0	2.1	82.9	55.9
2	B	350	0.69	—	4.25	0.93	1.5	9.9	1.0	0.0	0.0	1.5	86.1	62.1
3	B	375	0.69	—	4.25	0.82	1.8	23.6	1.3	0.0	0.0	1.2	72.2	48.3
4	B_1	350	0.58	—	4.25	1.08	2.4	1.9	2.4	0.0	0.8	1.1	91.3	77.0
5	B_2	350	0.58	—	4.25	1.16	1.5	0.0	1.8	0.0	0.0	2.3	94.5	85.0
6	B_3	350	0.58	—	4.25	1.09	3.0	0.0	1.0	0.0	0.0	0.5	95.5	80.5
7*	B_2	350	0.60	N 1 : 1	4.25	1.20	1.7	0.0	0.0	0.0	0.0	4.3	94.1	86.6
8*	B_2	350	0.60	N 1 : 3.5	4.25	1.20	1.2	0.0	0.0	0.0	0.0	2.8	96.0	87.6
9	B_2	350	0.60	H_2O; 1 : 13	4.25	1.20	2.4	0.3	1.0	0.0	0.0	1.3	95.0	88.5
10	B_4	350	0.60	—	3.67	0.81	5.3	0.5	1.1	0.7	0.0	1.6	90.5	61.4
11*	B_4	350	0.60	N 1 : 3.5	3.26	0.83	6.1	0.0	0.7	0.4	1.7	4.4	88.5	74.1
12	F	270	0.21	—	4.25	1.08	2.1	0.0	0.8	0.0	1.0	0.0	96.1	81.8
13	F_{Ca}	305	0.70	H_2O; 1 : 10	4.08	0.84	4.6	1.7	1.2	0.5	0.0	—	93.5	63.6
14	F_{Ca}	330	0.70	H_2O 1 : 10	3.26	0.64	7.6	0.0	1.1	0.5	—	—	91.1	58.9
15	F_{Ca}	425	0.70	H_2O 1 : 10	4.08	0.82	3.4	1.7	2.7	0.2	3.4	—	88.5	58.8

*In Expt. Nos. 7, 8 and 11 the volume of nitrogen-free gas was considered.

$$CH_3-CH=CH-CH_2OH \longrightarrow CH_3-CH_2-CH_2-CHO$$

$$CH_3-CH_2-CH_2-CHO + CH_3-CH=CH-CH_2OH \longrightarrow CH_3-CH_2-CH_2-CH_2OH +$$
$$+ CH_3-CH=CH-CHO$$

$$CH_3-CH_2-CH_2-CH_2OH \longrightarrow CH_3-CH_2-CH=CH_2 + H_2O$$

Similar cases of the isomerization of α,β-unsaturated alcohols are described in the literature [15]. For example, allyl alcohol at 300° over aluminum oxide is converted to propionaldehyde.

$$CH_2=CH-CH_2OH \longrightarrow CH_3-CH_2-CHO$$

Together with butadiene, a small amount of butylenes is also formed from crotyl alcohol when the dehydrating component B of the S. V. Lebedev catalyst is used (Table 2, Expts. 1-3). Their probable formation is explained by the scheme given above.

In contrast to the American authors [6], we failed to find any indication that silica gel is a highly active catalyst for the dehydration of crotyl alcohol. Using a mixture of silica gel and tantalum pentoxide (2% Ta_2O_5 + 98% SiO_2), the yield of butadiene in the experiments where the crotyl alcohol was diluted with nitrogen proved to be large. It is known that a silica gel-tantalum catalyst of the above indicated composition is used in the synthetic rubber industry in the U.S.A. to obtain butadiene from a mixture of ethyl alcohol and acetaldehyde [14, 16].

$$C_2H_5OH + CH_3CHO \longrightarrow CH_2=CH-CH=CH_2 + 2H_2O$$

According to Quattlebaum [17] and some other authors [6], the reaction proceeds in two stages: 1) crotonization of the acetaldehyde $CH_3CHO + CH_3CHO \longrightarrow CH_3-CH=CH-CHO + H_2O$ and 2) deoxidation of the crotonaldehyde by ethyl alcohol to butadiene $CH_3-CH=CH-CHO + CH_3CH_2OH \longrightarrow CH_2=CH-CH=CH_2 + CH_3CHO + H_2O$.

It is possible to assume that the preparation of butadiene from crotonaldehyde proceeds in the given case through the intermediate stage of forming crotyl alcohol, i.e., not only deoxidation of the crotonaldehyde by ethyl alcohol occurs (associated with the removal of oxygen from crotonaldehyde), but also a related dehydrogenation with subsequent dehydration.

$$CH_3-CH=CH-CHO + CH_3CH_2OH \longrightarrow CH_3-CH=CH-CH_2OH + CH_3CHO$$

$$CH_3-CH=CH-CH_2OH \longrightarrow CH_2=CH-CH=CH_2 + H_2O$$

The results obtained by us show that when a silica gel-tantalum catalyst is used the yield of butadiene from crotyl alcohol (when the alcohol is diluted with nitrogen) is as high as 83 mole %, based on alcohol passed through. This circumstance permits the postulation that the preparation of butadiene from a mixture of ethyl alcohol and acetaldehyde on a silica gel-tantalum catalyst, the same as in the S. V. Lebedev process, can proceed through the stage of formation and subsequent dehydration of crotyl alcohol.

EXPERIMENTAL

Crotyl Alcohol was obtained by the reduction of crotonaldehyde with aluminum isopropoxide [18]; b. p. 120-121.5°, d_4^{20} 0.8502; n_D^{20} 1.4270; α-naphthylurethan, m. p. 95°.

Found %: N 5.85. $C_{15}H_{15}O_2N$. Calculated %: N 5.81.

TABLE 3

Catalytic Dehydration of Crotyl Alcohol Over Magnesium Sulfate, Aluminum Oxide and Silica Gel-Containing Catalysts

Expt. No.	Catalyst	Expt. temp. (°C)	Admittance (ml/hr/ml catalyst)	Diluent and degree of dilution (mole)	Alcohol passed (g)	Air-free gas (l, stand. conditions)	Composition of gas (volume %)							C_4H_8 on alcohol passed (mole %)
							CO_2	$C_4H_6+C_3H_6$	C_2H_4	CO	H_2	CH_4	C_4H_8	
1	$MgSO_4$	230°	0.28	—	4.08	0.53	3.2	2.4	1.5	0.7	1.2	—	91.2	39.2
2	$MgSO_4$	260	0.28	—	4.08	0.84	3.6	1.5	1.3	0.6	0.0	2.9	90.5	61.5
3	$MgSO_4$	285	0.28	—	4.08	0.73	5.1	0.5	1.4	0.7	2.1	—	87.0	51.5
4	$MgSO_4$—2	270	0.45	—	4.08	0.85	6.9	0.0	1.2	0.2	0.0	0.0	93.2	64.2
5*	$MgSO_4$—2	270	0.45	N 1:3	4.08	1.03	2.1	1.7	1.6	0.0	0.0	0.0	92.5	77.1
6*	$MgSO_4$—2	300	0.45	N 1:3	4.08	1.09	1.7	0.8	1.5	0.0	1.3	0.0	93.9	82.8
7*	$MgSO_4$—2	330	0.45	N 1:3	4.08	1.09	1.3	1.3	0.9	0.4	0.0	0.0	96.0	84.8
8	AOA (NIUIF)**	380	0.56	—	4.08	0.77	4.8	19.0	2.6	1.4	0.4	2.4	66.0	41.2
9	AOA (Dneprodzerzhinsk)	380	0.53	—	4.08	0.68	4.1	34.3	0.0	1.5	4.1	2.3	50.1	27.6
10	SiO_2	350	0.53	—	4.25	0.35	1.6	0.0	1.6	0.0	0.0	2.8	94.0	25.7
11	SiO_2	375	0.51	—	4.25	0.32	0.0	0.0	1.0	0.0	0.0	3.0	96.0	23.8
12	SiO_2+Ta_2O_5	350	0.53	—	4.08	0.81	0.9	4.4	1.2	0.0	1.3	2.8	87.6	57.5
13	SiO_2+Ta_2O_5	370	0.53	—	4.08	0.86	1.4	8.9	1.9	0.2	0.8	3.1	83.6	58.2
14*	SiO_2+Ta_2O_5	370	0.53	N 1:3	4.08	1.12	3.6	2.2	0.7	0.0	0.0	1.1	91.8	83.3

*In Expt. Nos. 5-7 and 14 the volume of nitrogen-free gas was considered.

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According to the literature data for crotyl alcohol: b. p. 121.5-122°, d_4^{20} 0.8490, n_D^{20} 1.42591 [19]; for α-naphthylurethan: m. p. 91-93° [6].

Apparatus and Method of Operation. The experiments on the dehydration of crotyl alcohol were run using a small laboratory catalysis apparatus. A quantz tube, containing 26 ml of catalyst, was inserted into a vertical catalysis furnace 25 cm high. A layer of fine quartz, serving as the vaporizer, was sifted over the catalyst layer. First it was established that crotyl alcohol is not decomposed on quartz under the experimental conditions used. To measure the temperature in the reaction zone the hot junction of a chromel-alumel thermocouple was placed in the center of the catalyst in the quartz container. A special apparatus, described earlier [20], was used to add the alcohol at a uniform rate from the injector.

In the experiments where the crotyl alcohol was diluted with water the latter was fed from a separate dropping device, while when nitrogen was used for dilution the rate of its passage was regulated using a rheometer. The liquid reaction products were condensed using condensers and then collected in an ice-cooled receiver. The gas was collected in a gasholder over saturated sodium chloride solution. After completing the passage of crotyl alcohol, water (about 3-5 ml) was fed into the furnace to displace the reaction products. The gaseous products were analyzed using the apparatus designed by VTI (All-Union Heat Engineering Institute). The amount of butadiene in the gas was determined by bromination (based on the weight of tetrabromobutane) and by the amount of maleic anhydride adduct. The tetrabromide of butadiene after recrystallization from alcohol had m. p. 117°. According to [21]: m. p. 118°.

The results of the catalytic conversion of crotyl alcohol are summarized in Tables 2 and 3.

Using the dehydrating component B_2 of the S. V. Lebedev catalyst, which favors the formation of butadiene from crotyl alcohol in maximum yield, we ran a series of experiments at 350° in order to accumulate and study the liquid conversion products. The experiments were run with a passage rate of 10 ml/hour/ml catalyst. A total of 102 g of crotyl alcohol was passed through. The obtained condensate consisted of two layers. Distillation of the lower water layer gave a fraction with b. p. 82-98°. The distillate was salted out with potash. The separated upper layer was added to the upper layer of the condensate, and the mixture was dried over potash. The dried product (42.26 g) was fractionated through a rectification column into the following fractions: 1st b. p. 76-87°, 2.33 g; 2nd b. p. 87-94°, 0.64 g, n_D^{20} 1.4110; 3rd b. p. 94-98°, 3.56 g, n_D^{20} 1.4181; 4th b. p. 98-118°, 2.21 g, n_D^{20} 1.4249, 5th b. p. 118-121°, 18.40 g, n_D^{20} 1.4282, residue and losses, 15.11 g.

The main portion of fraction 3 (94-98°, d_4^{20} 0.8329) distilled at 96.5°, which corresponds to methylvinylcarbinol. Literature data for methylvinylcarbinol: b. p. 97.2-97.3°, d_4^{20} 0.8318, n_D^{20} 1.4127 [19]. Treatment of the fraction with b. p. 94-98° with α-naphthyl isocyanate gave the urethan, which after recrystallization from petroleum ether was obtained as fine, pale yellow needle crystals with m. p. 93.5°. The mixed melting point with the α-naphthylurethan of crotyl alcohol was strongly depressed (69°). The amount of nitrogen in the obtained α-naphthylurethan was determined by Dumas microanalysis.

Found %: N 5.81. $C_{15}H_{15}O_2N$. Calculated %: N 5.81.

Information on the melting point of the α-naphthylurethan of methylvinylcarbinol is absent in the literature. Due to this we dehydrated 1,3-butylene glycol [22] to yield methylvinylcarbinol (b. p. 96-98°, d_4^{20} 0.8381, n_D^{20} 1.4120) and then prepared the α-naphthylurethan from it with m. p. 94°. The mixture of α-naphthylurethans, obtained from methylvinylcarbinol and from the fraction with b. p. 94-98°, melted at 93.5°.

The 5th fraction corresponds to unreacted crotyl alcohol.

In another portion of the crude condensate, after drying over fused $CuSO_4$, the amount of carbonyl compounds was determined quantitatively by the use of hydroxylamine hydrochloride. The amount of carbonyl compounds, calculated on the basis of C_4H_6O (either crotonaldehyde or methyl vinyl ketone, the presence of which is the most probable), was 0.12%.

SUMMARY

1. The equilibrium constants of the reaction for the dehydration of crotyl alcohol to butadiene were calculated, and from them the yields of reaction products in the temperature interval 300-800°K. From an approximate thermodynamic calculation it follows that thermodynamic limitations do not exist for the given

reaction. The yield of butadiene from crotyl alcohol increases when the temperature is raised and reduced pressure is employed.

2. A number of catalysts for the dehydration of crotyl alcohol to butadiene were examined. The best results were obtained using one of the dehydrating components, namely B_2, of the S. V. Lebedev catalyst, and here the yield of butadiene was 85-88.5 mole %, based on alcohol passed through.

3. The liquid products obtained in the catalytic dehydration of crotyl alcohol over catalyst B_2 were found to contain methylvinylcarbinol, formed as the result of crotyl alcohol isomerization.

4. The obtained results agree with the ideas regarding the scheme for the formation of butadiene from ethyl alcohol by the S. V. Lebedev method, according to which crotyl alcohol is an intermediate product in this process.

LITERATURE CITED

[1] German Patent 263,016 (1913); Chem. Zentr. II, 729 (1913).

[2] L. P. Kyriakides, J. Am. Chem. Soc. 36, 980 (1914).

[3] Ch. Prevost, Ann. Chim. (10), 10, 113 (1926).

[4] H. Nagai, J. Soc. Chem. Ind. Japan, 46, 1264 (1943).

[5] Iu. A. Gorin, J. Gen. Chem. 19, 877 (1949).*

[6] H. E. Jones, E. E. Stahly and B. B. Corson, J. Am. Chem. Soc. 71, 1822 (1949).

[7] Iu. A. Gorin, J. Gen. Chem. 16, 283, 1089 (1946).

[8] J. G. M. Bremner and G. D. Thomas, Trans. Farad. Soc. 44, 230 (1948).

[9] V. B. Fal'kovskii, J. Gen. Chem. 18, 1639 (1948).

[10] J. G. M. Bremner and G. D. Thomas, Trans. Farad. Soc. 43, 779 (1947).

[11] F. G. Brickwedde, M. Moskow and J. G. Aston, J. of Research, 37, 263 (1946).

[12] J. W. Reppe, Acetylene Chemistry, N. Y., 10 (1949).

[13] D. V. Tishchenko, Author's Certificate 46571 (1936).

[14] B. B. Corson, H. E. Jones, C. E. Welling, J. A. Hinckley and E. E. Stahly, Ind. Eng. Ch. 42, 359 (1950).

[15] P. E. Weston and H. Adkins, J. Am. Chem. Soc. 50, 1930 (1928).

[16] W. J. Toussaint, J. T. Dunn and D. R. Jackson, Ind. Eng. Ch. 39, 120 (1947).

[17] W. M. Quattlebaum, W. J. Toussaint and J. T. Dunn, J. Am. Chem. Soc. 69, 593 (1947).

[18] W. G. Young, W. H. Hartung and F. S. Crossley, J. Am. Chem. Soc. 58, 100 (1936).

[19] J. Baudrenghien, Bull. Soc. Chim. Belg. 31, 160 (1922).

[20] A. M. Levit and L. Kh. Freidlin, Factory Labs. 16, 244 (1950).

[21] S. V. Lebedev, Life and Works [in Russian] (ONTI, Khimteoret, 1938), p. 476.

[22] S. F. Birch and D. T. McAllan, J. Chem. Soc. 1951, 2556.

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REACTION OF ALKYLENE SULFIDES WITH HALIDES OF CARBOXYLIC ACIDS

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The reaction of alkylene sulfides with the halides of carboxylic acids has been studied but slightly up to now. It was only quite recently that studies were made of the reaction of ethylene sulfide with the chlorides of some aliphatic and aromatic carboxylic acids [1-3].

We studied the reaction of ethylene sulfide and of propylene sulfide with acetyl bromide, acetyl iodide, with the chlorides of mono-, di- and trichloroacetic acids, and with the bromides and iodides of other acids.

Acyl halides readily add to alkylene sulfides with the formation of the corresponding 2-haloalkyl thiolcarboxylates

$$R{-}CH{-}CH_2 + R'COX \longrightarrow RCHClCH_2SCOR'$$
$$\quad\quad\ \ S$$

The acyl chlorides add at a slower rate than do the corresponding bromides and iodides. Thus, if the chlorides add to alkylene sulfides when the reactants are mixed and heating is required to complete the reaction, then when the bromides, and especially the iodides, are added to alkylene sulfides the reaction proceeds so vigorously that cooling is required. For this reason the addition of the carboxylic acid bromides and iodides to alkylene sulfides was made in dry carbon tetrachloride medium and with cooling. Here reaction was practically complete immediately after all of the alkylene sulfide had been added to the acid halide.

It should also be mentioned that the longer the hydrocarbon chain of the acid halide, the slower the reaction with the alkylene sulfide and the smaller the yield of the corresponding 2-haloalkyl thioester.

The reaction of propylene sulfide with acid halides can proceed in two directions to yield either the 2-halo-n-propyl thioester (I) or the 2-halo-isopropyl thioester (II).

$$CH_3{-}CH{-}CH_2 + RCOX \begin{cases} \longrightarrow RCOSCH_2CHXCH_3 & \text{(I)} \\ \longrightarrow RCOSCH(CH_3)CH_2Cl & \text{(II)} \end{cases}$$
$$\quad\quad\ \ S$$

The direction of this reaction was studied on the example of adding acetyl iodide to propylene sulfide.

To determine the direction of the reaction we used the method of comparing the melting point of the crystalline derivative of the product obtained from the reaction of propylene sulfide with acetyl iodide with that of the corresponding compound of known structure.

To obtain the crystalline derivative we added the reaction product of propylene sulfide with acetyl iodide to trimethylamine

$$(CH_3)_3N + CH_3COSC_3H_6I \longrightarrow (CH_3)_3\overset{+}{N}{-}C_3H_6SCOCH_3\ \overset{-}{I}$$

The 2-(acetothio)propyltrimethylammonium iodide obtained in this manner had m. p. 234°.

Acetyl β-methylthiocholine iodide $(CH_3)_3\overset{+}{N}\overset{}{\underset{I^-}{}}-CH_2CH(CH_3)SCOCH_3$, synthesized by the Renshaw method [4], has m. p. 144-145°. Its mixture with the 2-(acetothio)propyltrimethylammonium iodide obtained by us melted at 131°, i.e., it gave a sharp depression.

As a result, the obtained substance proved to be different from acetyl β-methylthiocholine iodide. It should have only one possible structure, namely that of acetyl α-methylthiocholine iodide $(CH_3)_3\overset{+}{N}\overset{}{\underset{I^-}{}}-CH(CH_3)-CH_2SCOCH_3$. The formation of a substance with such a structure is possible if propylene sulfide is cleaved by acetyl iodide according to direction (I) with the formation of 2-iodo-n-propyl thiolacetate.

EXPERIMENTAL

Preparation of 2-Chloroethyl Trichlorothiolacetate. Three grams of ethylene sulfide was placed in a round-bottomed flask fitted with reflux condenser and dropping funnel. Nine grams of trichloroacetyl chloride was gradually added from the dropping funnel to the alkylene sulfide at the boil. After all of the chloride had been added the reaction mixture was heated at 60° for 1.5 hours. The obtained 2-chloroethyl trichlorothiolacetate was vacuum-distilled. Yield 9 g (75%).

B. p. 88-89° (3 mm), d_4^{17} 1.5492, n_D^{17} 1.5351. MR_D 48.41; calc. 48.29.

Found %: Cl 58.21; S 12.97. $C_4H_4OCl_4S$. Calculated %: Cl 58.00; S 13.26.

The other 2-chloroalkyl thiolcarboxylates were obtained in similar manner.

Preparation of 2-chloropropyl chlorothiolacetate. For reaction we took 11.3 g of chloroacetyl chloride and 7.4 g of propylene sulfide. We obtained 12.4 g (67%) of compound.

B. p. 85° (2.5 mm), d_4^{18} 1.3125, n_D^{18} 1.5201, MR_D 43.35; calc. 43.00.

Found %: Cl 38.06; S 16.58. $C_5H_8OCl_2S$. Calculated %: Cl 37.99; S 17.16.

Preparation of 2-chloropropyl dichlorothiolacetate. For reaction we took 5 g of propylene sulfide and 7 g of dichloroacetyl chloride. We obtained 7 g (63%) of compound.

B. p. 90° (2 mm), d_4^{18} 1.3651, n_D^{18} 1.4995, MR_D 47.50; calc. 49.94.

Found %: Cl 47.53; S 14.40. $C_5H_7OCl_3S$. Calculated %: Cl 48.02; S 14.51.

Preparation of 2-chloropropyl trichlorothiolacetate. For reaction we took 5 g of propylene sulfide and 8 g of trichloroacetyl chloride. We obtained 7.6 g (67%) of compound.

B. p. 95° (2 mm), d_4^{18} 1.4345, n_D^{18} 1.5048, MR_D 52.206; calc. 52.834.

Found %: Cl 54.75; S 12.78. $C_5H_6OCl_4S$. Calculated %: Cl 55.38; S 12.52.

Preparation of 2-bromoethyl thiolacetate. A mixture of 20 g of acetyl bromide and 30 ml of dry carbon tetrachloride was placed in a round-bottomed flask fitted with reflux condenser and dropping funnel. Then, with water-cooling, 10.5 g of ethylene sulfide was added gradually from the dropping funnel. After all of the sulfide had been added the reaction mixture was heated at 60° for 20 minutes, the solvent removed by distillation, and the 2-bromoethyl thiolacetate vacuum-distilled. Yield 21 g (70%).

B. p. 78° (10 mm), d_4^{19} 1.5330, n_D^{19} 1.5220, MR_D 36.20; calc. 36.22.

Found %: Br 44.0; S 17.20. C_4H_7OBrS. Calculated %: Br 43.7; S 17.50.

The other 2-haloalkyl thiolcarboxylates were obtained in similar manner.

Preparation of 2-bromoethyl bromothiolacetate. For reaction we took 12 g of bromoacetyl bromide, twenty ml of carbon tetrachloride and 3.6 g of ethylene sulfide. We obtained 10 g (64.5%) of substance with b. p. 117° (5 mm), d_D^{21} 1.928.

Found %: Br 61.40; S 12.00. $C_4H_6OBr_2S$. Calculated %: Br 61.10; S 12.20.

Preparation of 2-bromoethyl thiolpropionate. For reaction we took 7 g of propionyl bromide, 15 ml of carbon tetrachloride and 3 g of ethylene sulfide. We obtained 9 g (90%) of 2-bromoethyl thiolpropionate.

B. p. 97° (16 mm), d_4^{17} 1.4285, n_D^{17} 1.5220, MR_D 41.60; calc. 40.87.

Found %: Br 40.82; S 16.03. C_5H_9OBrS. Calculated %: Br 40.6; S 16.25.

Preparation of 2-bromoethyl thiolbutyrate. For reaction we took 15.1 g of butyryl bromide, 25 ml of carbon tetrachloride and 6 g of ethylene sulfide. We obtained 16 g (76%) of 2-bromoethyl thiolbutyrate.

B. p. 102° (13 mm), d_4^{20} 1.3294, n_D^{20} 1.500. MR_D 46.38; calc. 45.48.

Found %: Br 38.15; S 14.86. $C_6H_{11}OBrS$. Calculated %: Br 37.9; S 15.14.

Preparation of 2-bromoethyl thiolbenzoate. For reaction we took 9 g of benzoyl bromide, 10 ml of carbon tetrachloride and 2.9 g of ethylene sulfide. We obtained 6.5 g (54.6%) of 2-bromoethyl thiolbenzoate with b. p. 153° (13 mm) (partial decomposition) and d_4^{19} 1.4850.

Found %: Br 32.88; S 12.87. C_9H_9OBrS. Calculated %: Br 32.63; S 13.05.

Preparation of 2-bromopropyl thiolacetate. For reaction we took 6.7 g of acetyl bromide, 15 ml of carbon tetrachloride and 4 g of propylene sulfide. We obtained 10 g (85%) of 2-bromopropyl thiolacetate.

B. p. 58° (3 mm), d_4^{10} 1.4220, n_D^{10} 1.5110, MR_D 41.40; calc. 40.87.

Found %: Br 40.81; S 16.00. C_5H_9OBrS. Calculated %: Br 40.6; S 16.25.

Preparation of 2-iodopropyl thiolacetate. For reaction we took 14 g of acetyl iodide, 20 ml of carbon tetrachloride and 6.1 g of propylene sulfide. We isolated 14.2 g (70.5%) of 2-iodopropyl thiolacetate.

B. p. 85° (8 mm), d_4^{22} 1.5465, n_D^{22} 1.5030, MR_D 44.10; calc. 45.10.

Found %: I 52.15, S 12.95. C_5H_9OIS. Calculated %: I 52.00; S 13.12.

Preparation of 2-bromopropyl bromothiolacetate. For reaction we took 12 g of bromoacetyl bromide, 30 ml of carbon tetrachloride and 4.4 g of propylene sulfide. We obtained 8 g (48.8%) of 2-brompropyl bromothiolacetate with b. p. 124° (7 mm), d_4^{20} 1.7560.

Found %: Br 58.20; S 11.45. $C_5H_8OBr_2S$. Calculated %: Br 57.91; S 11.6.

Preparation of 2-bromopropyl thiolpropionate. For reaction we took 7 g of propionyl bromide, 10 ml of carbon tetrachloride and 4 g of propylene sulfide. We isolated 8 g (72.5%) of 2-bromopropyl thiolpropionate.

B. p. 100° (15 mm), d_4^{20} 1.3425, n_D^{20} 1.5010, MR_D 46.35; calc. 45.48.

Found %: Br 38.06; S 15.00. $C_6H_{11}OBrS$. Calculated %: Br 37.94; S 15.16.

Preparation of 2-bromopropyl thiolbutyrate. For reaction we took 8 g of butyryl bromide and 4 g of propylene sulfide. We obtained 8.5 g (71%) of 2-bromopropyl thiolbutyrate.

B. p. 110° (14 mm), d_4^{18} 1.2745, n_D^{18} 1.4920, MR_D 51.05; calc. 50.10.

Found %: Br 35.83; S 14.01. $C_7H_{13}OBrS$. Calculated %: Br 35.6; S 14.22.

Preparation of 2-bromopropyl thiolbenzoate. For reaction we took 10 g of benzoyl bromide and 4 g of propylene sulfide. We obtained 6 g (43%) of 2-bromopropyl thiolbenzoate with b. p. 158° (15 mm) (partial decomposition) and d_4^{20} 1.3850.

Found %: Br 31.17; S 12.14. $C_{10}H_{11}OBrS$. Calculated %: Br 30.9; S 12.36.

Preparation of 2-(acetothio)propyltrimethylammonium iodide. A mixture of 14 g of 2-iodopropyl thiolacetate, obtained by the reaction of acetyl iodide with propylene sulfide, and 25 ml of dry ether was placed in a round-bottomed flask. Three grams of trimethylamine was gradually added to the solution cooled to -10°.

After all of the amine had been added the reaction mixture was allowed to stand in the cold for 5-6 hours and then for another 3 days at room temperature. The obtained precipitate of 2-(acetothio)-propyltrimethylammonium iodide was filtered and then recrystallized three times from butanol. After 3 recrystallizations we obtained 8.6 g (50.6%) of substance with m. p. 234°.

Found %: N 3.4; I 35.5; S 10.2. $C_8H_{18}ONIS$. Calculated %: N 4.6; I 35.3; S 10.5.

A mixture of this compound with acetyl β-methylthiocholine iodide, obtained by the Renshaw method, melted at 131-134°.

SUMMARY

1. Ethylene sulfide and propylene sulfide were reacted with the chlorides of di- and trichloroacetic acids, and with the bromides of acetic, bromoacetic, propionic, butyric and benzoic acids. The corresponding compounds were obtained.

2. The new compounds-chloroethyl trichlorothiolacetate, 2-chloropropyl chlorothiolacetate, 2-chloropropyl dichlorothiolacetate, 2-chloropropyl trichlorothiolacetate, 2-bromoethyl thiolacetate, 2-bromoethyl bromothiolacetate, 2-bromoethyl thiolpropionate, 2-bromoethyl thiolbutyrate, 2-bromoethyl thiolbenzoate, 2-bromopropyl thiolacetate, 2-bromopropyl bromothiolacetate, 2-bromopropyl thiolpropionate, 2-bromopropyl thiolbutyrate, 2-bromopropyl thiolbenzoate and acetyl α-methylthiolcholine iodide were synthesized and described.

3. It was determined that acetyl iodide adds to propylene sulfide with the formation of 2-iodo-n-propyl thiolacetate.

LITERATURE CITED

[1] U. S. Patent 2,212,141; Chem. Zentr. 1941, I, 446.

[2] E. Meade and F. Woodward, J. Chem. Soc. 1948, 1894.

[3] C. Culvenor, et al., J. Chem. Soc. 1949, 282.

[4] S. Z. Ivin, J. Gen. Chem. 22, 267 (1952).*

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REACTION OF HALIDES OF CARBOXYLIC ACIDS WITH ALIPHATIC α-OXIDES

S. Z. Ivin

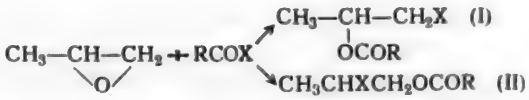
Only a few studies, devoted to the reaction of halides of carboxylic acids with aliphatic α-oxides, are known in the literature. Thus, for example, the reaction of acetyl chloride and acetyl iodide with ethylene oxide [1], of acetyl bromide with propylene oxide [2], and of acetyl chloride with epichlorohydrin [3], are described.

We made a more detailed study of the reaction of some bromides and iodides of carboxylic acids with ethylene oxide, propylene oxide and epichlorohydrin.

Acid bromides and iodides readily add to alkylene oxides with the formation of the corresponding 2-haloalkyl carboxylic acid esters according to the scheme

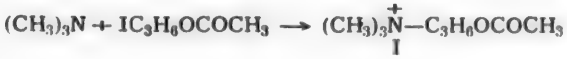
The reactions were run in anhydrous carbon tetrachloride medium with ice-water cooling. The addition of the acid halides to alkylene oxides is practically complete by the time all of the α-oxide has been added to the acid halide. The resulting 2-haloalkyl carboxylic esters were obtained as pure compounds, and their yields reached 70-85%.

The reaction of propylene oxide with acid halides can proceed in two directions with the formation of either the 2-haloisopropyl carboxylate (I) or the 2-halo-n-propyl carboxylate (II).



The direction of this reaction was studied on the example of adding acetyl iodide to propylene oxide. To determine the direction of reaction we used the method of comparing the melting point of the crystalline derivative of the reaction product between propylene oxide and acetyl iodide with the melting point of the corresponding compound of known structure.

To obtain the crystalline derivative we added the reaction product of propylene oxide with acetyl iodide to trimethylamine in known manner [4].



The 2-acetopropyltrimethylammonium iodide obtained in this manner melted at 175° and proved to be identical with 2-methylacetylcholine iodide $(CH_3)_3\overset{+}{N}CH_2\overset{CH_3}{\overset{|}{C}}HOCOCH_3\ \overline{I}$, which according to the literature has m. p. 174° [5]. A mixture of these two compounds failed to show a melting point depression.

The identity of the synthesized methylacetylcholine iodide with 2-methylacetylcholine iodide indicates that the reaction product of acetyl iodide with propylene oxide was 2-iodoisopropyl acetate (I). Consequently, the addition of acetyl iodide to propylene oxide proceeds by the first direction

$$CH_3-CH-CH_2 + CH_3COI \rightarrow CH_3-\underset{OCOCH_3}{\underset{|}{CH}}-CH_2I$$
$$\quad\ \ O$$

EXPERIMENTAL

Preparation of 2-bromoethyl acetate. A mixture of 20 g of acetyl bromide and 30 ml of dry carbon tetrachloride was placed in a round-bottomed flask fitted with reflux condenser and dropping funnel. Then 7.2 g of ethylene oxide was added in drops with ice-water cooling.

When all of the ethylene oxide had been added the reaction mixture was heated at 40-50° for 20 minutes. The formed 2-bromoethyl acetate was vacuum-distilled. Yield 20 g (74%).

B. p. 160° (750 mm), d_4^{25} 1.502, n_D^{25} 1.457. MR_D 30.20; calc. 30.08.

Found %: C 28.6; H 4.4; Br 48.21. $C_4H_7O_2Br$. Calculated %: C 28.8; H 4.5; Br 48.0.

The other 2-haloalkyl carboxylates were prepared by the same method used to obtain 2-bromoethyl acetate.

Preparation of 2-bromoethyl bromoacetate. For reaction we took 10 g of bromoacetyl bromide, 20 ml of carbon tetrachloride and 2.1 g of ethylene oxide. We obtained 5.2 g (43%) of compound.

B. p. 85° (5 mm), d_4^{16} 1.970 n_D^{16} 1.526, MR_D 38.30; calc. 38.86.

Found %: C 19.31; H 2.3; Br 65.4. $C_4H_6O_2Br_2$. Calculated %: C 19.5; H 2.4; Br 65.0.

Preparation of 2-iodopropyl acetate. For reaction we took 25 g of acetyl iodide, 40 ml of carbon tetrachloride and 8.5 g of propylene oxide. We obtained 20 g (60%) of 2-iodopropyl acetate.

B. p. 64° (7-8 mm), d_4^{14} 1.6762, n_D^{14} 1.4900, MR_D 39.35; calc. 38.93.

Found %: C 26.2; I 55.8. $C_5H_9O_2I$. Calculated %: C 26.2; I 55.6.

Preparation of 2-bromopropyl propionate. For reaction we took 13.7 g of propionyl bromide and 5.8 g of propylene oxide. We isolated 16 g (82%) of compound.

B. p. 68° (12 mm), d_4^{18} 1.3253, n_D^{18} 1.4500, MR_D 39.25; calc. 38.34.

Found %: C 36.6; Br 41.4. $C_6H_{11}O_2Br$. Calculated %: C 36.9; Br 41.05.

Preparation of 2-bromoethyl benzoate. For reaction we took 15 g of benzoyl bromide and 4 g of ethylene oxide. We isolated 7.8 g (41%) of 2-bromoethyl benzoate with b. p. 130° (10 mm).

Found %: C 45.4; Br 35.2. $C_9H_9O_2Br$. Calculated %: C 45.6; Br 35.0.

Preparation of 2-bromoethyl propionate. For reaction we took 7 g of propionyl bromide and 2.2 g of ethylene oxide. We obtained 7.6 g (83%) of compound.

B. p. 67° (10 mm), d_4^{20} 1.3820, n_D^{20} 1.454. MR_D 35.01; calc. 34.71.

Found %: C 33.10; Br 44.30. $C_5H_9O_2Br$. Calculated %: C 33.2; Br 44.15.

Preparation of 2-bromoethyl butyrate. For reaction we took 8 g of butyryl bromide and 2.4 g of ethylene oxide. We isolated 8 g (77%) of 2-bromoethyl butyrate.

B. p. 75° (12 mm), d_4^{19} 1.3258, n_D^{19} 1.4510. MR_D 39.54; calc. 38.34.

Found %: C 36.56; Br 41.35. $C_6H_{11}O_2Br$. Calculated %: C 36.9; Br 41.05.

Preparation of 2-bromopropyl butyrate. For reaction we took 3.5 g of butyryl bromide and 0.8 g of propylene oxide. We obtained 2.6 g (60%) of compound.

B. p. 83° (14 mm), d_4^{20} 1.2568, n_D^{20} 1.438. MR_D 44.28; calc. 42.94.

Found %: C 40.00; Br 38.5. $C_7H_{13}O_2Br$. Calculated %: C 40.1; Br 38.3.

Preparation of 2-bromopropyl benzoate. For reaction we took 5.5 g of benzoyl bromide and 1.8 g of propylene oxide. We obtained 4.5 g (61%) of compound with b. p. 140° (12 mm) and d_4^{20} 1.3504.

Found %: C 49.19; Br 33.21. $C_{10}H_{11}O_2Br$. Calculated %: C 49.35; Br 32.9.

Preparation of 2-bromo-2-chloropropyl bromoacetate. For reaction we took 10 g of bromoacetyl bromide and 5 g of epichlorohydrin. We obtained 9 g (60%) of compound.

B. p. 115° (5 mm), d_4^{16} 1.901, n_D^{16} 1.5270, MR_D 49.10; calc. 48.34.

Found %: C 20.1; Br 54.45; Cl 12.20. $C_5H_7O_2Br_2Cl$. Calculated %: C 20.4; Br 54.36; Cl 11.85.

Preparation of 2-bromo-2-chloropropyl propionate. For reaction we took 7 g of propionyl bromide and 5.2 g of epichlorohydrin. We obtained 8.5 g (69%) of 2-bromo-2-chloropropyl propionate.

B. p. 96° (12 mm), d_4^{20} 1.4500, n_D^{20} 1.4750, MR_D 44.51; calc. 43.10.

Found %: C 31.1; Br 35.2; Cl 15.7. $C_6H_{10}O_2BrCl$. Calculated %: C 31.4; Br 35.00; Cl 15.50.

Preparation of 2-bromo-2-chloropropyl acetate. For reaction we took 10 g of acetyl bromide and 7.5 g of epichlorohydrin. We obtained 14 g (80%) of compound.

B. p. 93° (15 mm), d_4^{25} 1.536, n_D^{25} 1.4818, MR_D 40.00; calc. 39.58.

Found %: C 27.7; Br 37.5; Cl 16.75. $C_5H_8O_2BrCl$. Calculated %: C 27.9; Br 37.2; Cl 16.5.

Preparation of 2-chloro-2-iodopropyl acetate. For reaction we took 10 g of acetyl iodide and 5.4 g of epichlorohydrin. We obtained 12 g (78%) of compound.

B. p. 110° (15 mm), d_4^{16} 1.785, n_D^{16} 1.5240, MR_D 44.70; calc. 43.80.

Found %: C 22.68; I 48.2; Cl 13.75. $C_5H_8O_2ClI$. Calculated %: C 22.90; I 48.4; Cl 13.50.

Preparation of 2-bromo-2-chloropropyl benzoate. For reaction we took 9.3 g of benzoyl bromide and 5.2 g of epichlorohydrin. We obtained 7 g (48%) of 2-bromo-2-chloropropyl benzoate with b. p. 157-162° (10 mm) and d_4^{22} 1.4602.

Found %: C 40.41; Br 30.2; Cl 13.65. $C_{10}H_{10}O_2ClBr$. Calculated %: C 40.70; Br 30.00; Cl 13.40.

Preparation of 2-acetopropyltrimethylammonium iodide. Into a round-bottomed flask was placed 9.7 g of 2-iodopropyl acetate, obtained by the addition of acetyl iodide to propylene oxide, and 30 ml of dry ether.

To the solution, cooled to -15°, was gradually added 2.5 g of trimethylamine with shaking. When all of the amine had been added the flask was stoppered and allowed to stand in the cold for 4-6 hours and then for another 3 days at room temperature.

The obtained precipitate of 2-acetopropyltrimethylammonium iodide was filtered and recrystallized twice from butanol. We obtained 8.1 g (66%) of compound with m. p. 175°.

Found %: C 33.10; N 4.31; I 44.5. $C_8H_{18}O_2NI$. Calculated %: C 32.85; N 4.9; I 44.2.

A mixture of the obtained substance with acetyl β-methylcholine iodide $(CH_3)_3\overset{+}{N}\overset{}{\underset{I^-}{}}-CH_2CH(CH_3)OCOCH_3$ melted at 175°, i.e., the m. p. was not depressed.

SUMMARY

1. Ethylene oxide, propylene oxide and epichlorohydrin were reacted with acetyl bromide, bromoacetyl bromide, acetyl iodide, propionyl bromide, butyryl bromide and benzoyl bromide.

2. The compounds 2-iodopropyl acetate, 2-bromopropyl propionate, 2-bromoethyl propionate, 2-bromoethyl butyrate, 2-bromopropyl butyrate, 2-bromopropyl benzoate, 2-bromo-2-chloropropyl bromoacetate, 2-bromo-2-chloropropyl propionate, 2-chloro-2-iodopropyl acetate and 2-chloro-2-bromopropyl benzoate were obtained for the first time and their properties characterized.

3. It was established that acetyl iodide adds to propylene oxide with the formation of 2-iodoisopropyl acetate.

LITERATURE CITED

[1] E. Gustus and P. Stevens, Zbl. 1933, I, 1929.

[2] R. Hunt and R. Renshaw, J. Pharm. a. exper. Therapie 51, 237 (1934).

[3] P. Truchot, Lieb. Ann. 138, 297 (1866); 140, 245 (1866).

[4] S. Z. Ivin, J. Gen. Chem. 22, 267 (1952).*

[5] R. Major and H. Bonnett, J. Am. Chem. Soc. 57, 2125 (1935).

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SULFONATION REACTION

XLVI. EQUILIBRIUM BETWEEN TOLUENETRISULFONIC ACID AND ITS TRICHLORIDE

A. A. Spryskov and Iu. L. Kuz'mina

It was shown earlier [1] that between sulfonic acids and their chlorides in a medium composed of a mixture of sulfuric and chlorosulfonic acids equilibrium is established according to the equation

$$RSO_2Cl + H_2SO_4 \rightleftarrows RSO_3H + HSO_3Cl$$

It was mentioned [1d] that as a rule the values of the equilibrium constants for the di- and trisulfonic acid derivatives are higher than for the monosulfonic acid derivatives.

Below we describe the results of studying the equilibrium for still another case involving polysulfonic acid derivatives, namely that of 2,4,6-toluenetrisulfonyl chloride with the corresponding trisulfonic acid in a mixture of sulfuric and chlorosulfonic acids. The toluenetrisulfonyl chloride (m. p. 162°), obtained by the earlier described method [2], was added to mixtures of chlorosulfonic and sulfuric acids of variable composition, contained in small ground-glass stoppered flasks. After the trichloride had dissolved the solutions were kept at a temperature of 80 ± 1°, and then the reaction mixtures were poured over ice. The deposited trichloride was filtered, washed, dried, and weighed. The reaction mixtures were kept at 80° for 10 hours, since from a series of experiments it was found that this length of time at 80° is sufficient to reach a condition close to equilibrium.

The chlorosulfonic acid used in the experiments had b. p. 86-88° at 20-25 mm, and contained 2.4% sulfuric acid.

As had already been shown by us earlier [1c], for the case of polysulfonic acid derivatives equilibrium is established between the polysulfonyl chloride and the sulfonyl chloride of the sulfonic acid. The equilibrium constant for the trisulfo derivatives of toluene is calculated starting with the equation

$$CH_3C_6H_2(SO_2Cl)_3 + H_2SO_4 \rightleftarrows CH_3C_6H_2(SO_2Cl)_2SO_3H + HSO_3Cl,$$

i.e., the disulfonyl chloride of the sulfonic acid is formed, which can then suffer further transformation to the sulfonyl chloride of the disulfonic acid, and then to the trisulfonic acid by the equations:

$$CH_3C_6H_2(SO_2Cl)_2SO_3H + H_2SO_4 \rightleftarrows CH_3C_6H_2(SO_2Cl)(SO_3H)_2 + HSO_3Cl,$$
$$CH_3C_6H_2(SO_2Cl)(SO_3H)_2 + H_2SO_4 \rightleftarrows CH_3C_6H_2(SO_3H)_3 + HSO_3Cl$$

The transformations according to the last two equations either proceed at a much slower rate than does the transformation according to the first equation, or else the equilibrium constants of the last two reactions are exceedingly small.

If for 1 mole of the trisulfonyl chloride we take m moles of sulfuric acid and n moles of chlorosulfonic acid, then the equilibrium constant based on the first equation is determined by the formula

$$k = \frac{[x][n+x]}{[1-x][m-x]},$$

where x corresponds to the number of moles of the trisulfonyl chloride converted to the disulfonyl chloride of the sulfonic acid.

The experimental results given in Table 1, permit determining the equilibrium constant, and from this it becomes possible to calculate the values of x using the formula

$$x = \frac{n+k+km \pm \sqrt{(n+k+km)^2 - 4(k-1)km}}{2(k-1)}$$

The computed values of x are given in the last column of Table 1, and as can be seen, differ from the experimentally found values (Column 4, Table 1) by approximately 1-2%.

TABLE 1

Equilibrium Between 2,4,6-Toluenetrisulfonic Acid and Its Trichloride at 80 ± 1°

Expt. Nos.	Moles /1 mole chloride		Chloride isolated (%)	Equilibrium constant k	Cl computed by the formula (%)
	H_2SO_4	HSO_3Cl			
212	1.04	9.51	83.7	2.15	82.0
219	1.32	9.53	79.7	2.23	78.0
216	3.86	13.32	60.3	2.61	61.3
217	3.42	12.46	60.2	2.81	62.5
215	4.32	12.34	55.5	2.64	56.7
213	4.31	10.23	51.9	2.59	51.3
			Average	2.50	

DISCUSSION OF RESULTS

We studied a total of 8 cases of equilibrium between sulfonic acids and their chlorides starting with the chloride which, in a mixture of sulfuric and chlorosulfonic acids, is converted to the sulfonic acid up to equilibrium. In practice it is usually necessary to convert the sulfonic acids or their sodium salts to the chlorides. The sulfonic acids are converted directly to the chlorides in the sulfonation mass obtained by adding the sulfonic acid in question to chlorosulfonic acid. The sodium sulfonates are converted to the chlorides by adding the dry salt to chlorosulfonic acid.

The found equilibrium constants reveal that sulfonic acids behave quite differently in their conversion to chlorides. Thus, polysulfonic acids, possessing as a rule higher equilibrium constants, are converted to the chlorides in smaller yields than are the monosulfonic acids.

In Table 2 we give the results of calculating the yield of chloride, starting with the sulfonic acid, when 5 moles of chlorosulfonic acid are taken per sulfonic group, and also the amount of chlorosulfonic acid required to give the chloride in 90% yield. In all previously described experiments we started with the chloride, sulfuric acid and chlorosulfonic acid. In order to be able to utilize all of the earlier used formulas, we conditionally

brought all of the substances to the same original state. Thus, 1 mole of sulfonic acid with 5 moles of chlorosulfonic acid is conditionally converted completely to 1 mole of the chloride and 1 mole of sulfuric acid, while 4 moles of chlorosulfonic acid remain. This mixture is now reacted to the equilibrium state. The given data reveal that to obtain a high yield of polysulfonyl chloride it is frequently necessary to take very large amounts of chlorosulfonic acid.

We also compared the yields of chloride obtained when the sulfonic acid and its sodium salt were reacted with chlorosulfonic acid. The reaction of 1 mole of sodium 2,5-dichlorosulfonate with 5 moles of chlorosulfonic acid and 0.005 mole of sulfuric acid gives the chloride in 79% of the theoretically possible yield, as is shown by calculation using the method published in the paper devoted to a study of the equilibrium between the sodium sulfonate or the sulfonic acid and the chloride [3]. The yield of chloride from the free sulfonic acid under the same conditions reaches 87.8%. Consequently, to obtain the same yields of chloride from sodium sulfonates requires larger amounts of chlorosulfonic acid than when the corresponding free sulfonic acids are used.

TABLE 2

Conversion of Sulfonic Acids to Their Chlorides

Acid	k	Using 5 moles HSO_3Cl / sulfonic group (%)	HSO_3Cl required / sulfonic group to give 90% Cl yield (moles)
m-Nitrobenzenesulfonic acid	0.51	90.0	5.0
2,5-Dichlorobenzenesulfonic acid	0.64	88.9	6.1
p-Toluenesulfonic acid	1.18	81.4	10.5
m-Sulfobenzoic acid	1.22	81.0	10.8
2,4-Toluenedisulfonic acid	0.90	83.0	17.3
1,3-Benzenedisulfonic acid	1.33	77.7	24.6
1,3,5-Naphthalenetrisulfonic acid	1.90	70.5	52.5
2,4,6-Toluenetrisulfonic acid	2.50	65.3	68.2

However, in practice high yields of the chlorides are obtained even when a much smaller excess of chlorosulfonic acid than that indicated above is used. This happens in the cases where the formed chloride precipitates from solution, as a result of which the equilibrium is shifted in the direction of forming more chloride.

SUMMARY

The equilibrium between 2,4,6-toluene trisulfonic acid and its trichloride was studied in a medium composed of chlorosulfonic and sulfuric acids, at 80°. The equilibrium constant was found to be 2.50.

It was shown that to obtain equal yields of the chlorides, starting with polysulfonic acids, requires larger amounts of chlorosulfonic acid per sulfonic group than when starting with monosulfonic acids. To obtain an equal yield of the chloride from the sodium sulfonates requires larger amounts of chlorosulfonic acid than when the corresponding free sulfonic acids are used.

LITERATURE CITED

[1] A. A. Spryskov and Iu. L. Kuz'mina, a) J. Gen. Chem. 21, 714 (1951);* b) J. Gen. Chem. 21, 1887 (1951);* c) J. Gen. Chem. Suppl. I, 559 (1953);* d) J. Gen. Chem. 23, 1536 (1953).*

[2] A. A. Spryskov and T. I. Iakovleva, J. Gen. Chem. 25, 783 (1955).*

[3] A. A. Spryskov and N. V. Apar'eva, J. Gen. Chem. 25, 2286 (1955).*

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REACTION OF SOME ORGANOSILICON COMPOUNDS WITH CELLULOSE NITRATES

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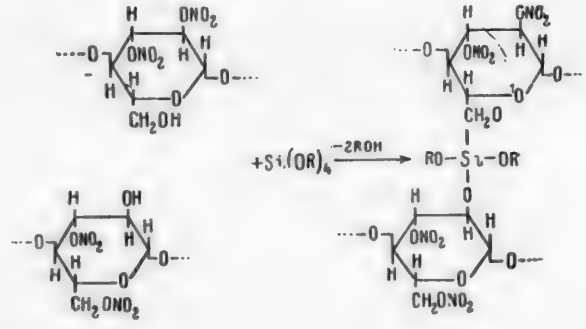
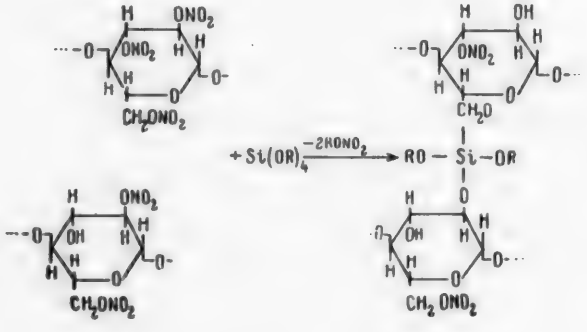
We had shown [1-6] that alkoxy- and alkoxyhalosilanes, alkyl and arylalkoxysilanes, alkyl-arylhalosilanes and the products of their hydrolytic cleavage and subsequent condensation, and also many other mono-, di-, tri- and tetrafunctional organosilicon compounds show double decomposition reaction with various inorganic and organic compounds, containing in their molecule either active atoms or functional groups (H, Cl, OH, OR, NH_2, etc.). The products obtained in this manner prossess valuable properties [7-10]. Such products, for example, are the high-molecular compounds based on organosilicon compounds and cellulose nitrate, obtained for the first time in the D. I. Mendeleev Moscow Chemical Technological Institute [11], which compounds possess high hydrophobicity, high heat and acid resistance, and good electrical insulation properties [12-15]. However, the processes for the reaction of organosilicon compounds with cellulose nitrates have remained unstudied right up to now.

The present paper is devoted to a study of the indicated reaction. Our investigations revealed that depending on the conditions the following processes are observed. 1) Exchange reaction of the starting organosilicon compounds with the free hydroxyl groups of the cellulose nitrate, accompanied by the joining together of the nitrocellulose macromolecule and the silicon atoms through the oxygen



2) Transesterification of the nitrate ester



The formation of more complex coupling products of organosilicon compounds with cellulose nitrates is possible, observed when the reaction is run in the presence of hydrogen chloride.

EXPERIMENTAL

The starting cellulose nitrate was pyroxylin containing 11.89% nitrogen, 0.50% moisture and 0.3% ash. As the starting organosilicon compounds we used various tetraalkoxysilanes and alkylalkoxysilanes, synthesized and purified by methods described in the literature [15]. The physical constants of all of the starting compounds agreed with the literature data.

It had been established by us [11] that the heating of cellulose nitrate solutions in a mixed solvent (for example, in a mixture of acetone, ethyl acetate and methyl alcohol, taken in the mole ratio 1 : 0.2 : 2.5) with tetraalkoxysilanes and alkylalkoxysilanes, and also with the products of their chemical transformations, leads to the formation of siliconitrocellulose compounds. The method given below was used by us to isolate and study the individual fractions of the compounds obtained in this manner. A mixture of 50 g of the starting pyroxylin and 450 g of acetone was placed in a three-necked flask, fitted with an oil-seal mechanical stirrer and thermometer. The mixture was stirred until a homogeneous acetone solution of cellulose nitrate was obtained. Then the obtained solution was maintained with constant stirring on the water bath at 55-57° for 3-18° hours. After this the flask contents were cooled and decanted into a beaker containing benzene. The obtained mixture was allowed to stand for 15 hours. Here a precipitate of cellulose nitrate deposited. The isolated precipate was pressed, broken up, and dried in a steam chest for 6 hours at 95-97°. The dried cellulose nitrate was subjected to elemental analysis.

Found %: N 11.31; C 28.40; H 3.40. $C_6H_7O_2(ONO_2)_{2.06}(OH)_{0.94}$. Calculated %: N 11.32; C 28.24; H 3.12.

Using similar conditions, a solution of pyroxylin, heated to 55°, was treated with various esters of orthosilicic acid in an amount corresponding to a mole ratio of $C_6H_7O_2(ONO_2)_2OH : Si(OR)_4$ equal to 1 : 1. The time of heating ranged from 5 to 15 hours. The analysis data for the obtained products reveal that the amount of silicon in the product increases gradually the longer the acetone solution of cellulose nitrate is heated with the tetraethoxysilane. The amount of silicon in the obtained products reaches 0.3-0.55%, and the nitrogen content 11.32-11.25%.

In order to remove the organosilicon compounds the obtained products were reprecipitated three times and then washed with benzene. The analysis data for the washed products, and for those obtained from the mother liquor, revealed that both had practically the same silicon and nitrogen content.

By means of special experiments with tetraethoxysilane it was observed that even traces of chlorosilanes exert a sharp influence on the reaction of tetraethoxysilane with cellulose nitrate. The elementary composition of the reaction products obtained under these conditions differed sharply from the elementary composition of the products synthesized from chemically pure compounds.

In order to study the reaction of other esters of orthosilicic acid with cellulose nitrates, and also to study the influence of chloroderivatives of silane on the process, we ran a series of experiments with chemically

TABLE 1

Elementary Composition of Reaction Products of Cellulose Nitrate with Alkoxysilanes, Containing $SiCl_4$

Formula of alkoxysilane	Elementary composition (%)			
	N	Si	C	H
$(CH_3O)_4Si$	9.76	7.65	28.52	3.32
$(C_2H_5O)_4Si$	10.64	3.75	29.18	3.13
n-$C_4H_9O)_4$ Si . . .	10.66	1.53	30.48	3.67
iso-$C_5H_{11}O)_4Si$ . . .	9.86	0.76	32.70	4.49

pure tetramethoxy-, tetraethoxy-, tetra-n-butoxy- and tetraisoamyloxysilanes, and with the same esters containing chloroderivatives. The reaction conditions were similar to those described above. The compounds, obtained by the reaction of chemically pure alkoxysilanes with cellulose nitrate, had a silicon content of the order of 0.15-0.7%. The elemental analysis data for the reaction products of cellulose nitrate with the indicated alkoxysilanes, containing 0.01% $SiCl_4$, are given in Table 1.

With increase in the amount of chloroderivatives in the alkoxysilanes the amount of nitrogen decreases, and the amount of silicon increases. The presence of large amounts of chloroderivatives in the starting alkoxysilanes leads to the formation of a solid insoluble compound, whereas the reaction products of the chemically pure alkoxysilanes with cellulose nitrates are soluble. Using similar conditions, we ran some experiments with a cellulose nitrate containing 12.39% nitrogen. Full compliance with the above described rules was also observed in this series of experiments.

We also ran some experiments with alkylalkoxysilanes that contained chlorosilanes. The analysis data for the obtained products are given in Table 2.

TABLE 2

Amount of Nitrogen and Silicon in Reaction Products of Cellulose Nitrate (11.87% N) with Alkylalkoxysilanes, Containing 0.01% $SiCl_4$

Formula of alkylalkoxysilane	N (%)	Si (%)
$(CH_3)_3Si(OCH_3)$	10.64	0.26
$(C_2H_5)_2Si(OCH_3)_2$	10.07	1.23
$(C_2H_5)_2Si(OC_2H_5)_2$	10.10	1.58

We also ran a series of experiments in which the various cellulose nitrates were heated with alkoxysilanes in the absence of a solvent. In the experiments with tetramethoxysilane the heating was at 110-120°, and in the experiments with tetraethoxysilane it was at 130-155°. The cellulose nitrate and orthosilicic ester were taken in such amount that all of the cellulose nitrate was found dissolved in the alkoxysilane. In all of the experiments the cellulose nitrate showed swelling clear up to gelatinization. The reaction products were pressed, repeatedly washed with benzene, and dried. In this series of experiments the evolution of the corresponding alcohol and of nitrogen oxides was observed, which can serve as evidence that the alkoxysilanes react with both the hydroxyl groups and the nitrate groups of cellulose nitrate. The elemental analysis data for the obtained products are given in Table 3.

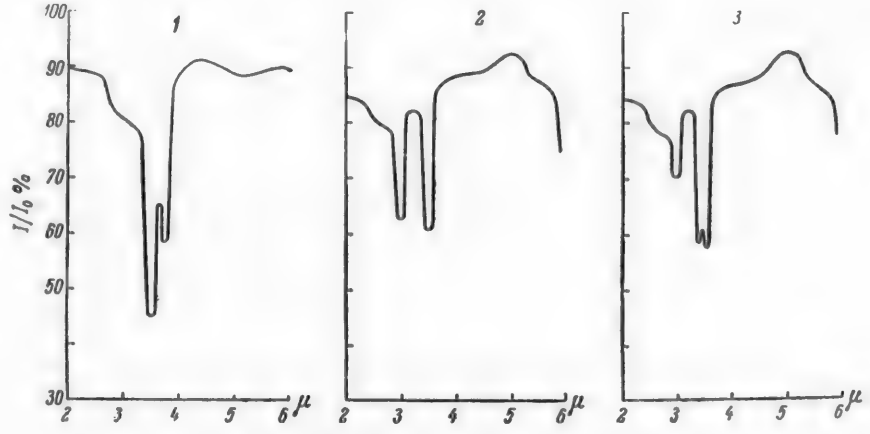
TABLE 3

Elementary Composition of Reaction Products of Alkoxysilanes with Cellulose Nitrate in Heterogeneous Medium

Formula of starting alkoxysilane	N in cellulose nitrate (%)	Elementary composition (%)			
		N	Si	C	H
$(CH_3O)_4Si$	11.89	10.03	3.24	29.43	3.72
	12.39	10.54	3.74	28.04	3.31
	13.36	10.80	6.56	28.12	3.23
$(C_2H_5O)_4Si$	11.89	9.26	1.52	30.72	3.70
	12.39	9.80	2.83	32.17	3.56
	13.36	11.20	1.59	29.68	3.21

The reaction of cellulose nitrate with alkoxysilanes, containing chloro derivatives, gave products with a nitrogen content of 7 to 11%, and a silicon content of 3 to 10%.

We also studied the infrared spectra of the reaction products of tetraethoxysilane with cellulose nitrate (11.87% N) The starting product contained 0.55% silicon. The investigation was run using an IKS-11 spectrometer and NaCl prism. The cellulose nitrate and its reaction product with tetraethoxysilane were studied as films, having a thickness of 19-20 μ, obtained from solutions of these products in acetone by evaporation of the solvent in vacuo. The spectrum of $(C_2H_5O)_4Si$ was taken as a 20% solution in CCl_4 in the interval of 2-6μ using a NaCl cuvette and a layer thickness of 0.1 mm. The absorption curves of cellulose nitrate, of tetraethoxysilane, and of their reaction product, are shown in the Figure. The absorption at 2.8-3 and at 3.5 μ is respectively due to the vibrations of the OH and CH groups [16-20]. In the given wavelength intervals, as well as throughout the whole spectrum, the absorption curve for the reaction product of tetraethoxysilane with cellulose nitrate shows all of the main characteristic absorption maxima, belonging to both cellulose nitrate and to tetraethoxysilane. A substantial reduction in the absorption maximum is observed at 3 μ. This permits the conclusion that the reaction of tetraethoxysilane with cellulose nitrate under the above indicated conditions proceeds with a reduction in the number of hydroxyl groups.



Infrared absorption curves. 1) Tetraethoxysilane, 2) cellulose nitrate, 3) cellulose nitrate, reacted with tetraethoxysilane.

After precipitating the product from acetone solution with benzene, the acetone-benzene mixture, obtained as a clear liquid, was fractionally distilled. The distillate, obtained from the first distillation, was fractionated through a column with an efficiency of 25 theoretical plates. The head fraction was shown to contain alcohols, corresponding to the starting alkoxysilane [20].

Using the method of ultraviolet spectroscopy, it was shown that, together with nitrogen oxides, an alkyl nitrate was present in the reaction products. This indicates that the nitrate groups of nitrocellulose react with the alkoxy groups of organosilicon compounds. Such a reaction course is in agreement with the studies of S. N. Danilov, who showed that under certain conditions the reaction of cellulose nitrate with acetic acid leads to replacement of the nitrate groups by the acetyl group [23].

We also determined the heats of swelling of the obtained products in acetone [21, 22] (cf. Table 4).

From the data of Table 4 it can be seen that the heats of swelling of the obtained compounds decrease with increase in the amount of silicon in them.

The solubility of the reaction products in various polar and nonpolar solvents, and in their mixtures, was studied. It was found that the solubility of the obtained products decreases with increase in the amount of silicon in them. The products containing up to 1% silicon are readily soluble in pyridine, acetone, alcohol-

ether mixtures, cyclohexanone, alkyl acetates, in mixtures of the latter with toluene and xylene, in nitrobenzene, and in camphor. Increasing the silicon content above 1% leads to a loss in the solubility of the products in the indicated solvents.

As a result, based on the obtained data it can be assumed that the indicated organosilicon compounds, react with the hydroxyl groups, and under certain conditions, also with the nitrate groups of cellulose nitrate, as is evidenced by the evolution of an alcohol and nitrogen oxides.

The presence of chlorosilane impurities in the alkoxy- and alkylalkoxysilanes hastens this process considerably, as can be judged by the amount of silicon in the obtained products.

It is known that the dissolving of cellulose nitrates is accompanied by the formation of chemical adducts between the functional groups of the cellulose nitrate and the solvent [24-26] and this process can be characterized by the heat effect of solution. A decrease in the heat of swelling with increase in the amount of silicon in the products obtained by us points to a reduction in the amount of active functional groups in the cellulose nitrate. Analysis of the obtained products by the method of infrared spectroscopy also indicates this. The solubility of cellulose nitrates to a considerable degree characterizes their structure. A reduction in the solubility of the products obtained by us with increase in their silicon content can be explained by the formation of chemical bonds in the reaction of the functional groups of cellulose nitrates with the alkoxy groups of organosilicon compounds, with the formation of compounds having a tridimensional structure in accordance with the schemes given above.

TABLE 4

Heats of Swelling of Reaction Products of Some Organosilicon Compounds with Cellulose Nitrate

Formula of starting organosilicon compound	Amount in product (%)		Heat of swelling (cal/g)
	N	Si	
Untreated cellulose nitrate . .	11.89	—	19.2
$(C_2H_5O)_4Si$	11.57	0.17	18.80
n-$(C_4H_9O)_4Si$ . . .	10.60	0.19	19.05
$(C_2H_5)_2Si(OC_2H_5)_2$.	10.05	1.50	15.88
$(C_2H_5O)_4Si$	10.48	4.75	15.01
$(CH_3O)_4Si$	8.50	5.65	14.90

SUMMARY

1. The reaction of tetramethoxy-, tetraethoxy-, tetra-n-butoxy-, tetraisoamyloxy-, trimethylmethoxy-, diethyldimethoxy- and diethyldiethoxysilanes with cellulose nitrates was studied.

2. The infrared spectra and heats of swelling of the reaction products of organosilicon compounds with cellulose nitrates were studied.

3. It was found that during the indicated reaction there occurs a reduction in the number of hydroxyl groups found in the elementary unit of the cellulose nitrate molecule, and also the liberation of an alcohol, both testifying to the fact that the reaction of alkoxysilanes and alkylalkoxysilanes with cellulose nitrates proceeds mainly as the result of reaction with the unesterified hydroxyl groups.

4. It was shown that under certain conditions a reduction in the amount of nitrogen in the reaction products is observed when compared to the starting cellulose nitrate, and also the evolution of nitrogen oxides during reaction, both testifying to the fact that the indicated reaction apparently also proceeds due to transesterification of the nitrate groups of the cellulose nitrate.

LITERATURE CITED

[1] A. P. Kreshkov, J. Gen. Chem. 17, 81 (1947).

[2] A. P. Kreshkov, Proc. Acad. Sci. USSR 59, 723 (1948).

[3] A. P. Kreshkov, Glass and Ceramics [in Russian], No. 5, 14 (1948).

[4] A. P. Kreshkov, G. S. Petrov and A. D. Saenko, J. Appl. Chem. (USSR) 22, 747 (1949).

[5] A. P. Kreshkov, J. Appl. Chem. (USSR) 23, 542 (1950).••

[6] A. P. Kreshkov, A. N. Chivikova, G. D. Nessonova, V. A. Matveev and M. L. Daroshkevich, Trans. D. I. Mendeleev Moscow Chem. Technol. Inst. 17, 15 (1952).

[7] G. S. Petrov, A. P. Kreshkov and A. D. Saenko, Author's Certificate 67, 925 (1946).

[8] A. P. Kreshkov and L. V. Anisimova, Trans. D. I. Medeleev Moscow Chem. Technol. Inst. 12, 35 (1947).

[9] A. P. Kreshkov and A. A. Latyshev, Author's Certificate 75, 516 (1948).

[10] A. P. Kreshkov and L. V. Anisimova, Author's Certificate 72, 873 (1948).

[11] A. P. Kreshkov, G. D. Nessonova and Ia. A. Gurvich, Author's Certificate 75, 517 (1948).

[12] A. P. Kreshkov, G. D. Nessonova, S. I. Malkov and B. D. Nessonov, Author's Certificate 77,000 (1948).

[13] A. P. Kreshkov and G. D. Nessonova, Registration Notice No. 1678-50-1 (1950).

[14] A. P. Kreshkov, S. I. Malkov, V. I. Matveev, G. D. Nessonova and V. D. Nessonov, Bull. Engr. Technol. No. 6, 278 (1952).

[15] A. P. Kreshkov, Organosilicon Compounds in Industry [in Russian] (State Industrial Construction Press, 1956), 2nd Edition.

[16] Lester P. Kuhn, Anal. Chem. 22, 282 (1950).

[17] J. C. D. Brand and T. M. Cawthon, J. Am. Chem. Soc. 77, 321 (1955).

[18] W. D. Kumler, J. Am. Chem. Soc. 75, 4346 (1953).

[19] V. N. Nikitin, J. Phys. Chem. (USSR) 23, 786 (1949).

[20] K. Bauer, Analysis of Organic Compounds [in Russian] (IL, 1953).

[21] S. P. Papkov, Dissertation: "Heat Effect of Reaction of Nitrocellulose with Solvents," Rayon Scientific Institute (1939).•

[22] E. Calvet, Bull. Soc. Chem. 1, 75 (1956).

[23] S. N. Danilov, M. A. Sokolovskii and A. I. Evdokimova, J. Gen. Chem. 17, 1888 (1947).

[24] V. A. Kargin and S. P. Papkov, J. Phys. Chem. (USSR) 7, 483 (1936).

[25] S. M. Lipatov and S. I. Meerson, Colloid J. (USSR) 12, 122 (1950).

[26] D. I. Gal'perin and L. I. Moseev, Colloid J. (USSR) 19, 167 (1957).••

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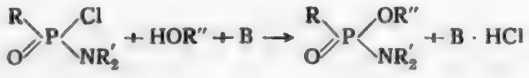
DERIVATIVES OF ALKYLPHOSPHONOUS AND PHOSPHONIC ACIDS

VIII. SYNTHESIS AND PROPERTIES OF SOME ALKYLATED AMIDES OF ALKYLPHOSPHONIC CHLORIDES

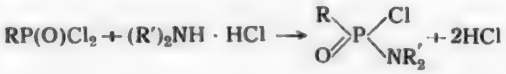
A. I. Razumov, O. A. Mukhacheva and E. A. Markovich

We studied several different routes for the synthesis of biologically active amide esters of alkylphosphonic acids. As it proved later, the best method was found to be the ammonolysis of the chlorides of alkylalkoxyphosphonic acids [1, 2]. However, in addition to the indicated method, we also studied the alkoxylation of the amides of alkoxyphosphonic chlorides with alcohols in the presence of either bases or alcoholates.



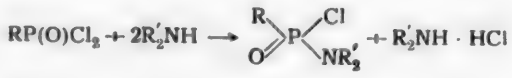
It was necessary to obtain the starting alkylated amides of the alkylphosphonic chlorides for the indicated syntheses. Similar compounds with mixed functions were studied quite extensively by Michaelis [3] for the case of phosphoric acid derivatives. These compounds were studied intensively both later and at the present time [4-8]. In recent years the attention of investigators has also been attracted to the corresponding fluoro derivatives [9-11]. Only a very small number of similar alkylphosphonic acid derivatives are known at the present time [12-13].

Two methods for the preparation of the alkylated amides of alkylphosphonic chlorides were studied. The first method consisted of the ammonolysis of the full chlorides of the acids with amine hydrochlorides of the Michaelis reaction, known for phosphoric acid derivatives [3].



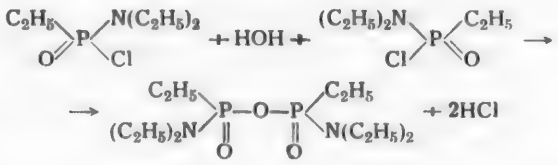
This method gives yields of the order of 30-35% and requires the use of at least 3 times the theoretical amount of the chloride, which for the most part is not recovered.

For this reason we gave preference to the method of partial ammonolysis of the full chlorides of primary phosphonic acids.



Using this method we obtained several members of this series of compounds (Table 1). The ammonolysis with primary amines gives products that cannot be vacuum-distilled; for this reason they were not isolated in a pure state.

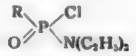
This first member of the amides (Table 1) is a crystalline substance (m. p. 42-43°) that can be vacuum-distilled with ease. The remaining members are liquids with a piercing mint or peppery odor. They fume in the air and are hydrolyzed with exceeding ease by atmospheric moisture. When reacted with water they cleave hydrogen chloride, while the phosphorus-containing radicals combine in pairs.



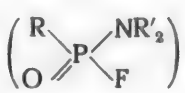
The yield of the obtained alkylpyrophosphonic amides is very small due to further reaction of the formed products with hydrogen chloride, which leads to cleavage of the amide groups and the formation of amine hydrochlorides due to the instability of the P—N bond in an acid medium. If sodium bicarbonate is added to the reaction mixture to bind the formed hydrogen chloride, then the yield of alkylpyrophosphonic acid derivatives rises to 50% and higher.

TABLE 1

Diethylamides of Alkylphosphonic Chlorides



R	B. p. (pressure in mm)	d_4^{20}	n_D^{20}	Analysis for Cl (%)		Analysis for P (%)		Yield (%)
				found	calc.	found	calc.	
CH_3	115—115.5° (9)	1.1274	1.4648	21.16	20.94	—	—	50
C_2H_5	101.5 (3.5)	1.0964	1.4643	—	—	16.59	16.89	65
n.-C_3H_7	112—113 (4)	1.0706	1.4642	—	—	15.43, 15.80	15.69	45
iso-C_3H_7	90—91 (1)	1.0707	1.4627	17.90	17.87	—	—	40
n.-C_4H_9	113—115 (3)	1.0526	1.4641	—	—	14.60, 14.90	14.65	50

The instability of the P—N bond is also manifested in the fluorination of the amides with sodium bifluoride, where the full alkylphosphonic fluorides $RP(O)F_2$ are formed simultaneously with the amides of the alkylphosphonic fluorides  due to rupture of the P—N bond. Consequently, in fluorination we isolated products of both the first and second type (Tables 2 and 3).

The alkylated amides of the alkylphosphonic fluorides are liquids with a faint aromatic odor. They are comparatively resistant to hydrolysis and possess a relatively high toxicity. The full alkylphosphonic fluorides are liquids with an astonishingly tenacious camphor-iodoform odor.

EXPERIMENTAL*

Preparation of Alkylated Amides of Alkylphosphonic Chlorides.

1. Ammonolysis of full alkylphosphonic chlorides with amine hydrochlorides. A mixture of 14 g of diethylamine hydrochloride and 60 g of ethylphosphonic chloride was heated in a flask with reflux condenser

* The experimental work was done in 1946-1947.

for 6 hours at 235°. The hydrogen chloride was absorbed in a Woulfe bottle containing water. The liquid assumed a brown color. The obtained product was vacuum-distilled. The yield was 7.5 g (35%). The other homologs were obtained in a similar manner.

2. Ammonolysis of full alkylphosphonic chlorides with free amines. The chloride, dissolved in approximately 6 volumes of dry ether, was placed in a flask fitted with reflux condenser, stirrer and dropping funnel. The amine, dissolved in an equal volume of ether, was added at -5°. After all of the amine had been added the reaction product was heated at solvent boil for 30-50 minutes. The hydrochloride was filtered, while the product was vacuum-distilled. All of the other homologs were obtained in a similar manner. It should be mentioned that the amount of hydrochloride obtained was always greater than the theoretical due to atmospheric moisture, which caused the reactions discussed in the general section of this paper. The amides of the phosphonic chlorides with a primary amine radical cannot be vacuum-distilled, for which reason they were used without distilling.

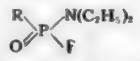
To run the ammonolysis we prepared the full alkylphosphonic chlorides (Table 4) by reacting phosphonic esters with phosphorus trichloride and chlorine. For this we usually took the butyl esters of various phosphonic acids. This method gives good yields.

Synthesis of Diethylpyrophosphonic Bis(Diethylamide).

1. Reaction of water with ethylphosphonic chloride diethylamide. The calculated amount of water was added with vigorous stirring in a rapid nitrogen stream to 46 g of the diethylamide at -10°. The product was quickly vacuum-distilled. The formation of a substantial amount of crystalline product was observed, which proved to be diethylamine hydrochloride (m. p. 217-219°). The yield of main product was 9%.

TABLE 2

Diethylamides of Alkylphosphonic Fluorides



R	B. p. (pressure in mm)	d_4^{20}	n_D^{20}	Analysis for P (%) found	Analysis for P (%) calc.	Yield (%)
CH_3	101° (19)	1.0735	1.4195	20.14, 20.20	20.26	33
C_2H_5	103 (15)	1.0036	1.4130	18.85	18.56	38
n-C_3H_7	110.5 (12)	1.0301	1.4238	17.45, 17.50	17.13	25
iso-C_3H_7	82 (17)	1.0263	1.4231	17.00, 16.85	17.13	34
n-C_4H_9	128—130 (16)	1.0380	1.4358	16.12, 16.29	15.89	30

2. Reaction of sodium bicarbonate with ethylphosphonic chloride diethylamide. For reaction we took 46 g of the amide and 21.5 g of sodium bicarbonate. The synthesis was run in nearly the same manner as described above. After removal of the sodium chloride the product was vacuum-distilled. The hydrochloride was also formed here, but only in small amount (0.2 g). The amount of main product obtained was 20 g (50%).

TABLE 3

Full Alkylphosphonic Fluorides $RP(O)F_2$

R	B. p. (pressure in mm)	d_4^{20}	n_D^{20}	Analysis for P (%) found	Analysis for P (%) calc.	Yield (%)
CH_3	22° (27)	1.3938	1.3277	31.08, 31.15	31.00	10
C_2H_5	44—45 (25)	1.2510	1.3410	26.7	27.10	25
n-C_3H_7	30.5 (13)	1.1791	1.3541	23.96, 23.92	24.21	34
iso-C_3H_7	25 (17.5)	1.1736	1.3512	23.93, 23.91	24.21	10
n-C_4H_9	51.5—52 (17.5)	1.1342	1.3709	21.63, 21.87	21.80	33

TABLE 4

Full Alkylphosphonic Chlorides $RP(O)Cl_2$

R	B. p. (pressure in mm)	Yield (%)
CH_3	59—59.5° (11.5)	90
C_2H_5	133.5—134.5 (15)	75
n-C_3H_7	141 (12.5)	75
iso-C_3H_7	113—114 (3)	70
n-C_4H_9	96—98 (15—16)	75

B. p. 163.5° – 164.5° at 2 mm, d_4^{20} 1.0619, n_D^{20} 1.4607, MR_D 80.68; calc. 80.57.

Found %: P 20.09; N 8.97, 9.00. $C_{12}H_{30}O_3N_2P_2$. Calculated %: P 19.87; N 8.97.

Fluorination of amides of phosphonic chlorides. The proper amide was charged into a Claisen flask, set up for distillation, and then the calculated amount of sodium bifluoride was added. The flask contents were heated to a definite temperature. On conclusion of reaction the product was distilled from the apparatus under a slight vacuum. The heating temperature for the methylphosphonic acid derivative was 110°, for the ethylphosphonic—135°, for the propylphosphonic—150°, and for the butylphosphonic—175°. The obtained mono- and difluoro derivatives were fractionally distilled. An attempt to use sodium fluoride for the fluorination with heating to 180° proved unsuccessful; the product taken for reaction was recovered unchanged.

SUMMARY

1. Some members of the alkylphosphonic acids with mixed functions were synthesized: the alkylated amides of phosphonic chlorides and fluorides, and also the full alkylphosphonic fluorides.

2. It was shown that the alkylated amides of phosphonic chlorides hydrolyze with ease and also that the P—N bond in the alkylated amides of phosphonic fluorides is unstable.

3. The ease with which the alkylated amides of phosphonic chlorides are hydrolyzed by moisture leads to the easy formation of the alkylated amides of alkylpyrophosphonic acids, while the instability of the P—N bond in the amides of phosphonic fluorides leads to the formation of the full fluorides when the indicated amide fluorides are heated.

LITERATURE CITED

[1] A. I. Razumov, O. A. Mukhacheva and E. A. Markovich, J. Gen. Chem. 27, 2389 (1957).*

[2] A. I. Razumov, Author's Certificate No. 12,249 (1951).

[3] A. Michaelis, Lieb. Ann. 326, 129 (1903); 395, 129 (1912); 407, 290 (1915).

[4] W. Steinkopf, Ber. 41, 3571 (1908).

[5] S. Goldschmidt and F. Obermeier, Lieb. Ann. 588, 24 (1954).

[6] A. V. Kirsanov and V. P. Molosnova, J. Gen. Chem. 25, 772 (1955).*

[7] A. V. Kirsanov and N. A. Egorova, J. Gen. Chem. 25, 1140 (1955).*

[8] M. Pianka and B. Owen, J. Appl. Chem. 5, 525 (1955).

[9] R. Heap and B. Saunders, J. Chem. Soc. 1948, 1313.

[10] B. Holmstedt, Acta phisiol. Scand. 25, Suppl. 90, 1045 (1951).

[11] BIOS, Final Report, 745 (1947).

[12] A. Ia. Iakubovich and V. A. Ginzburg, J. Gen. Chem. 24, 1465 (1954).*

[13] M. Sartori, Chem. Revs. 48, 225 (1951).

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SOME ARYL DERIVATIVES OF CYANOTHIOUREA

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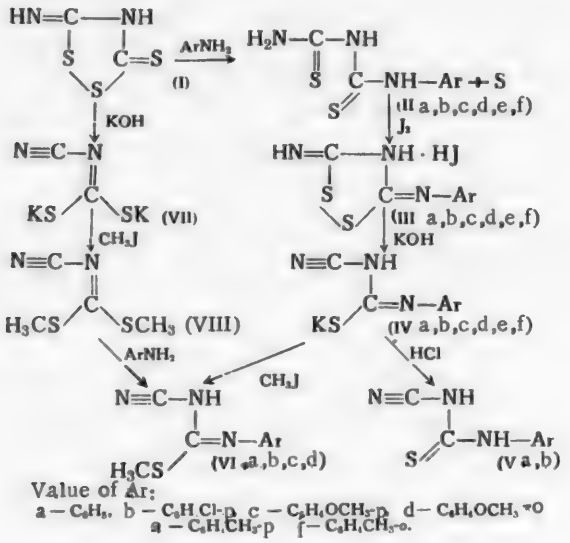
A number of thiourea compounds with biological activity are described in the literature [1]. For the most part recent studies have been devoted to derivatives of aminothiourea (thiosemicarbazide), among which were found compounds with antitubercular activity [2]. Other thiourea derivatives could alsobe of considerable interest, for example, those containing the physiologically active cyano group. In connection with this we decided to synthesize several N-aryl-N'-cyanothioureas (Ar−NH−CS−NH−C≡N).*



The starting substance for the synthesis of the indicated compounds was the readily available 5-imino-3-thio-1,2,4-dithiazolidine (isoperthiocyanic acid, "xanthane hydride") (I). This substance, obtained as early as 1821 by Wohler [3], is formed by the reaction of potassium thiocyanate with sulfuric acid in the cold. When 5-imino-3-thio-1,2,4-dithiazolidine is reacted with aromatic amines the heterocycle is cleaved with the elimination of elemental sulfur and 1-aryldithiobiurets are formed [4]. The dithiobiuret is easily oxidized, again suffering closure into a dithiazolidine compound (III) "thiuret" [5], which in turn when treated with potassium hydroxide is cleaved with the formation of the N-aryl-N'-cyanothiourea as the potassium salt having the iso form (IV).

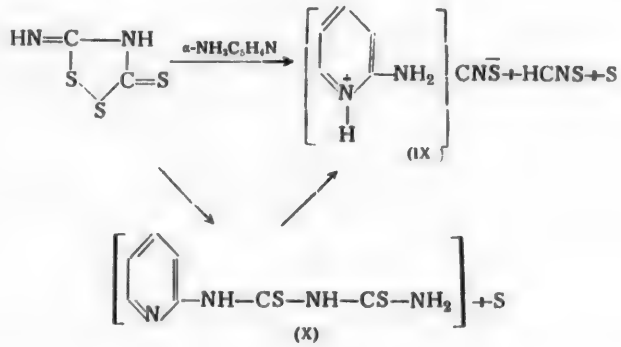
We obtained the potassium salts of the following compounds: N-phenyl- (IVa) [6], p-chlorophenyl- (IVb) [7], p-anisyl (IVc), o-anisyl- (IVd), p-tolyl- (IVe) and o-tolyl-isocyanothiourea (IVf). These salts when reacted with methyl iodide give readily crystallizing methyl esters (VI). These same esters can also be obtained by a shorter method from "xanthane hydride" (I): the reaction of potassium hydroxide with xanthane hydride gives the dipotassium salt of cyanamidodithiocarbonic acid (VII) in 85% yield [8], which when reacted with

* These compounds, having the cyano radical linked to the amino group, can also be regarded as being derivatives of cyanamide.

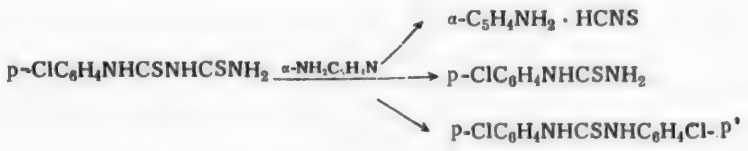
methyl iodide yields the dimethyl ester (VIII) [9]. When the latter is heated with arylamines the methyl esters (VI) are formed in good yields, in particular the p-anisidine compound (VIc), which is identical with the methylation product of the potassium salt of N-(p-anisyl)-N'-cyanoisothiourea.

The free cyanothioureas (V) could be of especial interest. They were isolated by the acidification of the corresponding isothiourea potassium salts (IV) with either hydrochloric or acetic acid. However, these compounds could not be obtained in the pure state, since they are easily changed even when heated in various solvents and migrate into compounds of unknown structure. The free N-phenyl-N'-cyanothiourea (Va) [10] and N-(p-chlorophenyl)-N'-cyanothiourea (Vb) [11] are mentioned in the literature. The N-(p-chlorophenyl)-N'-cyanothiourea (Vb) obtained by us has an ill-defined m. p. of 108-112° (decompn.) which is lower than that indicated in the literature [11]. To identify compound (Vb) we converted it to the potassium salt and then methylated with methyl iodide to give the ester, which proved to be identical with the methyl ester obtained from potassium salt (IVb). This suggests that in our case we were actually dealing with the free N-(p-chlorophenyl)-N'-cyanothiourea, and that the compound described in the literature [11], obtained by a different method, evidently represents a substance of different structure.

An attempt was made by us to obtain cyanothioureas (or the salts of their iso forms), containing instead of aryl either the heterocyclic pyridine or pyrimidine radical. In this connection we postulated that compounds of this nature could be of considerable interest for biological testing. However when α-aminopyridine, and also α-aminopyrimidine, was heated with "xanthane hydride," instead of the desired dithiobiurets we obtained the thiocyanic acid salts of α-aminopyridine (IX) and α-aminopyrimidine, respectively. The formation in these cases of thiocyanic acid salts instead of the α-pyridyl or α-pyrimidinyldithiobiuret can be explained either by the fact that "xanthane hydride" under the influence of either α-aminopyridine or α-aminopyrimidine is decomposed into 2 molecules of thiocyanic acid and sulfur, or by the fact that during the course of reaction the formed dithiobiuret of the heterocycle (X) is unstable and suffers decomposition under the influence of the α-aminoheterocycle.*



Such a reaction course is probably due to the ability of these heterocyclic amines to tautomerize. This postulation finds some support in the fact that even the stable p-chlorophenyldithiobiuret when heated with α-aminopyridine suffers cleavage with the formation of the thiocyanic acid salt of α-aminopyridine; at the same time some p-chlorophenylthiourea and N,N'-bis(p-chlorophenyl)thiourea are also formed.



* Soon after the conclusion of our work a paper [12] appeared in which a similar case of forming the thiocyanate of α-aminopyridine is mentioned. The mechanism of the reaction is not discussed in the paper.

Apparently, the basicity of the amine is not a decisive factor in this reaction, since when the reaction is run with ammonia, and also with isopropylamine, the p-chlorophenyldithiobiuret fails to suffer any changes.

In water solutions the potassium salts of arylcyanoisothioureas, and also the dipotassium salts of cyanamidodithiocarbonic acid, form precipitates with certain metal salts (cf. EXPERIMENTAL), which are either salts or possibly complex compounds. In connection with this the potassium salts could be of interest for physiological testing and also in analytical chemistry.

When tested in vitro the potassium salts of the cyanoisothioureas, and also the corresponding intermediate products, the dithiobiurets (II), showed only slight activity toward the virulent strain of tubercle bacillus (human type). •

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5-Imino-3-thio-1,2,4-dithiazolidine ("xanthane hydride") (I) was obtained by the described method [13] using potassium thiocyanate and sulfuric acid. The yield was 20-25% on the weight of potassium thiocyanate.

The aryl-dithiobiurets (II) were obtained, according to the literature data, by heating "xanthane hydride" with aromatic amines. The yields ranged from 60 to 65%. Melting point of phenyldithiobiuret 179-184° [12]), of p-chlorophenyldithiobiuret 167-168° (163-164° [14], 179-180° [12]), of p-anisyldithiobiuret 173-174° (173-174° [12]), of o-anisyldithiobiuret 142-143° (143-144° [12]), of p-tolyldithiobiuret 170-171° (173-174° [12]), and of o-tolyldithiobiuret 167° (159° [15]).

The 5-arylimino-3-imino-1,2,4-dithiazolidines (arylthiurets) (III) were obtained by the oxidation of the corresponding dithiobiurets with iodine in alcohol medium, using the Fromm method [16], and were isolated as the hydriodides. The products were purified by recrystallization from alcohol. The yields ranged from 70 to 90%. Melting points of hydriodic acid salts: phenylthiuret (IIIa) 157-158°, p-chlorophenylthiuret (IIIb) 229-230°, p-anisylthiuret (IIIc) 180-182° (182° [17]), o-anisylthiuret (IIId) 198-199° (199-200° [17]), p-tolylthiuret (IIIe) 217-218°, and o-tolylthiuret (IIIf) 143-145°.

Analysis Results.

(IIIa) — Found %: N 12.54. $C_8H_7N_3S_2 \cdot HI$. Calculated %: N 12.43. (IIIb) — Found %: N 11.35. $C_8H_6N_3S_2Cl \cdot HI$. Calculated %: N 11.30. (IIIc) — Found %: N 12.07. $C_9H_9N_3S_2 \cdot HI$. Calculated %: N 11.96. (IIId) — Found %: N 11.96. $C_9H_9N_3S_2 \cdot HI$. Calculated %: N 11.96.

Potassium salts of N-aryl-N'-cyanoisothioureas (IV). The thiuret hydriodide (III) (0.015 mole) was added with stirring to an ice cooled solution of 1 g of potassium hydroxide in 20 ml of water. After 30 minutes the deposited sulfur was filtered, and the filtrate was evaporated. The potassium salts (colorless needles) were obtained in quantitative yield. Melting points: (IVa) 201-202°, (IVb) 240-241°, (IVc) 218-226°, and (IVe) 232-234°.

Formation of precipitates in reaction of potassium salts with ions of some metals. To 2 ml of a 0.25 N solution of metal salt was added 2-3 drops of 0.1 M solutions of the investigated potassium salts of cyanamidodithiocarbonic acid (VII) and N-aryl-N'-cyanothioureas (IV). The characteristics of the obtained precipitates are given in Table 1.

N-phenyl-N'-cyanothiourea (Va). A suspension of 0.6 g of potassium salt (IVa) in 3 ml of ice-cooled 1 N hydrochloric acid was prepared. The suspension was filtered, and washed with cold water. We obtained 0.2 g of a yellow precipitate with m. p. 95-111° (decompn.). The substance is very soluble in hot alcohol. It decomposes when heated with water to a tarry product.

N-(p-chlorophenyl)-N'-cyanothiourea (Vb). A suspension of 0.85 g of potassium salt (IVb) in 3.2 ml of ice-cooled 1 N hydrochloric acid was prepared. The colorless crystalline precipitate was filtered and washed with cold water. The substance rapidly turns yellow in the air, m. p. 108-112° (decompn.) (157-158° [11]). When boiled in a mixture of alcohol and benzene it is converted to a crystalline substance of not investigated structure with m. p. 270-275° (decompn.). Treatment of the moist precipitate with 5% potassium hydroxide solution gave the potassium salt. The water solution of the potassium salt was evaporated to dryness on the

• We wish to thank E. I. Chertkova (Sverdlovsk Tuberculosis Institute) for testing the indicated compounds.

water bath, and the residue was heated for 1 hour with methyl iodide in alcohol medium. We obtained 0.6 g of the methyl ester of N-(p-chlorophenyl)-N'-cyanothiourea (VIb) as a crystalline product with m. p. 184°, not depressing the melting point when mixed with the methyl ester obtained from the potassium salt of N-(p-chlorophenyl)-N'-cyanoisothiourea (IVb).

Methyl esters of N-aryl-N'-cyanoisothioureas (VI). The N-aryl-N'-cyanoisothiourea potassium salt (IV) (0.02 mole) was heated for 1 hour with 0.03 mole of methyl iodide in 2-3 ml of alcohol. The solution was evaporated to dryness, made turbid with several milliliters of warm water, filtered, and the precipitate washed with water. All of the obtained esters crystallized readily from ethyl alcohol as colorless plates. The yields ranged from 42 to 52%. The melting points and analysis data are given in Table 2.

TABLE 1

Metal Salt	Starting compounds			
	(VII)	(IVa)	(IVb)	(IVc)
$Hg(NO_3)_2$	Colorless precipitate	Small amount of yellow precipitate, rapidly becoming colorless	Yellow precipitate, rapidly becoming colorless	Yellow precipitate, rapidly becoming colorless
$Zn(NO_3)_2$	Colorless precipitate	Colorless precipitate	Colorless precipitate	Colorless precipitate
$CD(NO_3)_2$	Colorless precipitate	Colorless precipitate	Colorless precipitate	Colorless precipitate
$Hg_2(NO_3)_2$	Brown precipitate	Brown precipitate	Light brown precipitate	Light brown precipitate
$Cu(NO_3)_2$	Brown precipitate Solution becomes green	Light-green precipitate, turning to a brown solution green	Brown precipitate turning to a light-green. Solution green.	Light-green precipitate. Solution green
$Bi(NO_3)_3$	Trace amount of yellow precipitate, turning orange	Brown precipitate, turning to an apricot-colored precipitate	Small amount of brown precipitate	Small amount of brown precipitate, turning to an apricot-colored precipitate. Solution yellow
$Pb(Ac)_2$	Yellow precipitate	Colorless precipitate	Yellow precipitate, turning colorless	Bright yellow precipitate, becoming colorless immediately
$ZrSO_4$	Slight turbidity	A colorless precipitate gradually appears	Slight turbidity, a colorless precipitate deposits gradually	Slight turbidity, a colorless precipitate deposits gradually
$AgNO_3$	Yellow precipitate, turning to a brown	The same as for compound (VII)		

Methyl ester of N-anisyl-N'-cyanoisothiourea (IVc). The dimethyl ester of cyanamidodithiocarbonic acid (m. p. 56-57°) (0.44 g), obtained by the procedure of [9], was heated on the water bath for 10 minutes with a solution of 0.37 g of p-anisidine in 3 ml of alcohol (sharp odor of mercaptan). The obtained precipitate after cooling was filtered and washed with a small amount of alcohol. Yield 0.5 g (76%), m. p. 181-182°. It fails to depress the melting point when mixed with the methyl ester of N-anisyl-N'-cyanoisothiourea (VIc), obtained from the potassium salt of N-anisyl-N'-isocyanothiourea (IVc).

Reaction of "xanthane hydride" with α-aminopyridine. A mixture of 3 g (0.02 mole) of "xanthane hydride" and 3.76 g (0.04 mole) of α-aminopyridine in 10 ml of alcohol was heated for 1 hour on the boiling water bath. The deposited sulfur was filtered and from the filtrate after cooling was isolated 5.1 g (84%) of the thiocyanic acid salt of α-aminopyridine. Colorless prisms from alcohol, m. p. 115-116°.

TABLE 2

Compounds	Empirical formula	Melting point	Found (%)		Calculated (%)	
			N	S	N	S
(VIa)	$C_9H_9N_3S$	185—186°	21.74	16.86	22.00	16.75
(VIb)	$C_9H_8N_3SCl$	184—185 (decompn.)	18.37	13.88	18.61	14.21
(VIc)	$C_9H_{11}N_3SO$	181—182	19.10	14.37	19.01	14.41
(VIe)	$C_{10}H_{11}N_3S$	148—149	20.77	—	20.48	—

Found %: N 26.88. $C_8H_7N_3S$. Calculated %: N 27.41.

When reacted with sodium hydroxide solution in the cold the substance yields the free α-aminopyridine and sodium thiocyanate. In a similar manner the reaction of α-aminopyrimidine with "xanthane hydride" gave a 77% yield of the thiocyanic acid salt of α-aminopyrimidine, obtained as colorless prisms; after recrystallization from alcohol, m. p. 137-138°.

Found %: N 36.15. $C_5H_6N_4S$. Calculated %: N 36.33.

Reaction of p-chlorophenyldithiobiuret with α-aminopyridine. A mixture of 3 g (0.012 mole) of p-chlorophenyldithiobiuret and 1.15 g (0.012 mole) of α-aminopyridine was heated for 1 hour in an oil bath at 125-130°. Within 10-15 minutes after the start of heating a test sample of the melt gave a distinct test for thiocyanic acid (red color with ferric chloride solution). At the end of heating the melt was shaken with 20 ml of water, filtered, and the precipitate on the filter washed well with water until all of the thiocyanic acid salt of α-aminopyridine had been removed (test with ferric chloride solution). Evaporation of the filtrate and wash waters led to obtaining 1.75 g (95%, based on taken α-aminopyridine) of the thiocyanate of α-aminopyridine, obtained as crystals with m. p. 115-116°. Three recrystallizations of the water-insoluble residue (0.60 g) from alcohol gave: 0.25 g of p-chlorophenylthiourea with m. p. 176-177° (175° [18]) and 0.1 g of N,N'-bis(p-chlorophenyl)thiourea with m. p. 168-170° (166-168° [18]).

Analysis results for p-chlorophenylthiourea and N,N'-bis(p-chlorophenyl)thiourea. Found %: N 14.65. $C_7H_7N_2SCl$. Calculated %: N 15.06. Found %: N 10.02. $C_{13}H_{10}N_2SCl_2$. Calculated %: N 9.46.

SUMMARY

1. The potassium salts and methyl esters of the iso forms of N-aryl-N'-cyanothioureas were obtained. Five-imino-3-thio-1,2,4-dithiazolidine ("xanthane hydride") was used as the starting material.

2. It was established that α-aminopyridine and α-aminopyrimidine, in contrast to aromatic amines, cleave "xanthane hydride" to yield thiocyanic acid salts of heterocyclic amines, and not dithiobiurets.

3. It was shown that the potassium salts of cyanamidodithiocarbonic acid and N-aryl-N'-cyanoisothioureas form water-insoluble precipitates with various metals.

4. The in vitro testing of the potassium salts of N-aryl-N'-cyanoisothioureas revealed that they were inactive toward tubercle bacillus.

LITERATURE CITED

[1] D. Schroeder, Chem. Revs. 55, 181 (1955).

[2] I. Ia. Postovskii and S. I. Omel'chenko, Prog. Chem. 22, 207 (1954); M. N. Shchukina and T. P. Sycheva, Chemistry of Science and Industry [in Russian] 1, 424 (1956).

[3] F. Wöhler, Ann. Physik, 69, 273 (1821).

[4] L. Glûtz, Lieb. Ann. 154, 44 (1870).

[5] E. Fromm, Lieb. Ann. 275, 20 (1893).

[6] A. Hantzsch and M. Wolvekamp, Lieb. Ann. 331, 265 (1904).

[7] A. Growther and F. H. S. Curd, J. Chem. Soc. 1948, 1639.

[8] A. Hantzsch and M. Wolvekamp, Lieb. Ann. 283, 28 (1894).

[9] A. Hantzsch and M. Wolvekamp, Lieb. Ann. 331, 290 (1904).

[10] A. Wunderlich, Ber. 19, 450 (1886).

[11] L. Fernandes and K. Ganapathi, Ch. A. 43, 5746 (1949).

[12] A. E. S. Fairfull and D. A. Peak, J. Chem. Soc. 1955, 796.

[13] F. D. Chattaway and H. P. Stevens, J. Chem. Soc. 71, 607 (1897).

[14] P. C. Guha and S. S. Guha, Ch. A. 46, 1039 (1952).

[15] E. Fromm and K. A. Schneider, Lieb. Ann. 348, 170 (1906).

[16] E. Fromm, Lieb. Ann. 275, 43 (1893).

[17] S. Swaminathan and P. C. Guha, Ch. A. 42, 3350 (1948).

[18] M. Shimotani, Ch. A. 47, 1627 (1953).

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MECHANISM OF THE REACTION OF TRANSAMINATION IN THE β-DIALKYLAMINOPROPIONITRILE SERIES

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Relative to the reaction discovered by us [1], and later by Bauer, Cymerman and Sheldon [2],* for alkyl-aryl transamination in the β-dialkylaminopropionitrile series

$$(Alk)_2NCH_2CH_2CN + Ar\overset{+}{N}H_3\bar{A}n = ArNHCH_2CH_2CN + (Alk)_2\overset{+}{N}H_2\bar{A}n$$

differences exist as to the mechanism of the process that takes place here. This reaction, leading to the formation of the β-arylaminopropionitrile, can be accomplished by two procedures.

1. The elimination of the dialkylamine with subsequent addition of the aromatic amine to acrylonitrile in the presence of the dialkylammonium salt, functioning as an acid catalyst.

$$(Alk)_2NCH_2CH_2CN + Ar\overset{+}{N}H_3\bar{A}n \rightarrow (Alk)_2\overset{+}{N}HCH_2CH_2CN\bar{A}n + ArNH_2$$

$$(Alk)_2\overset{+}{N}HCH_2CH_2CN\bar{A}n \rightarrow (Alk)_2NH + [\overset{+}{C}H_2CH_2CN]\,\bar{A}n;$$

$$[\overset{+}{C}H_2CH_2CN]\,\bar{A}n \rightarrow HAn + CH_2{=}CH{-}CN$$

$$(Alk)_2NH + HAn \rightarrow (Alk)_2\overset{+}{N}H_2\bar{A}n;$$

$$CH_2{=}CH{-}CN + ArNH_2 \xrightarrow[\text{catalyst}]{[(Alk)_2\overset{+}{N}H_2\bar{A}n]} ArNHCH_2CH_2CN$$

When a β-dialkylaminopropionitrile is reacted with a salt of an aromatic amine (hydrochloride, sulfate, acetate, etc.) a proton migrates to the β-dialkylaminopropionitrile as being the stronger base. The N-β-cyanoethyl-N,N-diethylammonium ion formed in this manner is unstable, due to the polarization of its bonds [3], and decomposes into diethylamine and acrylonitrile; the latter adds aromatic amine in the presence of an acid catalyst, when the dialkylammonium salt is at the reaction temperature.

2. The second procedure proposed is nucleophilic displacement or some similar reaction, where the hydrogen of the aromatic amine participates in the formation of the cleaved dialkylamine, i.e., a direct replacement of the dialkylamino group by the aromatic amine.

$$\bar{A}n\,(Alk)_2\overset{+}{N}HCH_2CH_2CN + ArNH_2 \rightarrow \bar{A}nAr\overset{+}{N}H_2CH_2CH_2CN + (Alk)_2NH \rightarrow$$

$$\rightarrow ArNHCH_2CH_2CN + \bar{A}n\overset{+}{N}H_2(Alk)_2$$

In opposition to this we believe that the reaction proceeds by the first scheme, i.e., cleavage of the N-β-cyanoethyl-N,N-dialkylammonium ion occurs first and this is followed by the addition of the aromatic amine to either the formed acrylonitrile or the carbonium ion.

*Our paper [1] was received by the editor on April 4, 1949, and that of the British authors [2] on June 14, 1951.

We had found [1] that the heating of β-diethylaminopropionitrile hydrochloride with aniline, or of the free base of the former with aniline hydrochloride, gives β-phenylaminopropionitrile in 64-67% yield. It proved that the hydrochloride of β-diethylaminopropionitrile is unstable and when heated decomposes into diethylamine hydrochloride and acrylonitrile. We ran the decomposition of the β-diethylaminopropionitrile hydrochloride in a Claisen flask with removal of the cleaved acrylonitrile by distillation, which was obtained by us in 77% yield.

Somewhat later Cymerman-Craig and co-workers [4], disputing this data, heated β-diethylaminopropionitrile hydrochloride in a flask under reflux and isolated 73% of unchanged β-diethylaminopropionitrile hydrochloride. Here they assumed that they had the conditions employed for the transamination reaction and concluded that the hydrochloride of β-diethylaminopropionitrile is stable. We are of the opinion that such a conclusion is without basis. The decomposition of β-diethylaminopropionitrile hydrochloride when heated is a reversible reaction

$$\bar{Cl}(C_2H_5)_2\dot{N}HCH_2CH_2CN \rightleftarrows \bar{Cl}(C_2H_5)_2\dot{N}H_2 + CH_2{=}CH{-}CN$$

and consequently it can be shifted in either direction depending on the concentration of the reactants in the reaction mixture. If acrylonitrile is removed from the reaction sphere (either by distillation or in the presence of aniline by reaction with the latter), then the reaction is shifted to the right. If the formed acrylonitrile and diethylamine hydrochloride remain in the reaction mixture, then the decomposition of the diethylaminopropionitrile hydrochloride proceeds only to establishing equilibrium. This conclusion is supported by experimental data. We found that diethylamine hydrochloride adds to acrylonitrile in anhydrous medium, i.e., under the conditions of the transamination reaction. By heating under reflux, Cymerman-Craig and co-workers [4] created conditions for establishing equilibrium in the reaction mixture at the experiment temperature, and this is the reason for their being able to obtain only a 27% decomposition of β-diethylaminopropionitrile hydrochloride.

That the mechanism for the discussed reaction corresponds to the first scheme is also supported by our experiment of heating aniline hydrochloride and β-diethylaminopropionitrile at 160°, run under conditions assuring the removal of volatile products. It was found that here the yield of cleaved acrylonitrile is only 47% (instead of 77%), and β-phenylaminopropionitrile is formed in 34% yield. These data permit the following explanation of the transformations that take place here: acrylonitrile, formed in the decomposition of the β-diethylaminopropionitrile, is partially removed by distillation and partially (possibly as a carbonium ion) adds aniline. This is the reason why only 47% of the acrylonitrile is removed by distillation, instead of the 77% obtained when the reaction is run in the absence of aniline. The obtained data clearly show that the process goes by the first scheme.

The instability of the hydrochloride of β-diethylaminopropionitrile and its tendency to decompose also appear at moderate temperatures, for example, when aqueous solutions of this salt are heated. It was found that the reaction for alkyl-aryl transamination can also proceed in water medium; here we obtained β-phenylaminopropionitrile in 50% yield. The heating of a water solution of β-diethylaminopropionitrile with removal of the volatile products by distillation also leads to decomposition of the taken nitrile into acrylonitrile and diethylamine (58%). These data also contradict the statement of Cymerman-Craig and co-workers [4] that β-diethylaminopropionitrile hydrochloride is stable.

As further evidence in support of the substitution mechanism (Scheme 2) the authors of [4] cite the fact that an aromatic amine hydrochloride when heated with acrylonitrile does not form the β-arylaminopropionitrile, whereas under the same conditions the hydrochloride of an aromatic amine reacts with β-diethylaminopropionitrile to give the β-arylaminopropionitrile in 78% yield. This conclusion also proves to be invalid, since we had established that the hydrochloride of an aromatic amine does not react with acrylonitrile in anhydrous medium and at low temperature (at the boiling point of acrylonitrile) for the reason that a proton is absent under these conditions, being a catalyst for the reaction (acrylonitrile is not a dissociating medium for an aromatic amine hydrochloride). The presence of an acid catalyst, for example diethylamine hydrochloride, suffering thermal dissociation under the experimental conditions (140-180°), assures the entrance of a proton into the reaction mixture.

It was found by us that an aromatic amine hydrochloride can add to acrylonitrile even when the heating is in aqueous medium, since apparently an aqueous medium, creating conditions for dissociation, assures the presence of a proton in the reaction mixture.

The possibility established by us of running the alkyl-aryl transamination reaction in aqueous medium and the fact that acrylonitrile adds to an aromatic amine hydrochloride in aqueous medium do not agree with the conclusions [4] that the substitution mechanism prevails here.

In a later paper [5] some data are presented, showing the relationship between the basicity of the aromatic amine and the yield of β-arylaminopropionitrile in the alkyl-aryl transamination reaction. The authors make the statement that the greater the basicity of the amine, the higher the yield of β-arylaminopropionitrile. The authors link this fact to the S_N2 mechanism [6] of nucleophilic displacement. However it should be mentioned, as had been shown by us earlier [7], that in the direct addition of aromatic amines to acrylonitrile the higher yields of β-arylaminopropionitriles are also associated with a greater basicity of the starting aromatic amine.

Interesting data, however not supporting the arguments of the indicated authors [5], were obtained by the latter when they introduced β-diethylamino-α-dimethylpropionitrile as one of the components in the discussed reaction. This compound, for structural reasons incapable of eliminating diethylamine and forming a double bond, is practically inert toward p-anisidine (the yield of product with unknown structure is a total of only 0.1%). In our opinion, this fact also strongly supports the theory that the reaction proceeds by way of elimination.

It was shown by Bauer and co-workers [2] that the alkyl-aryl transamination reaction does not go in the presence of BF_3, an acid catalyst. This circumstance also supports the conclusion that a proton-cleaving catalyst is necessary for the studied reaction.

Brewster and Eliel [8], discussing the alkylation mechanism of ammonium salts, came to the conclusion that the mechanism of the reaction consists in the cleavage of secondary amine with the formation of an unsaturated compound, which then adds the alkylating substance. They also consider the possibility of nucleophilic displacement less probable on the basis that the removal of a proton from the ammonium salt should proceed more easily than the displacement of a dialkylamine molecule.

Relative to the experiments made by the indicated authors [4] with deuterium, undertaken by them to prove the nucleophilic mechanism of the discussed reaction, it should be stated that the absence of analysis data for the deuterium content of the β-arylaminopropionitrile, and also the inadequate description of the experiments on the study and analysis of the diethylamine and water, unfortunately do not permit arriving at a conclusion as to the reliability of the arguments offered by Cymerman-Craig and co-workers [4].

Summarizing all of the above, we believe that the reaction of alkyl-aryl transamination in the β-dialkylaminopropionitrile series proceeds rather by way of cleavage of the dialkylamine and subsequent addition of the aromatic amine to the formed acrylonitrile (or to the carbonium ion) than by way of nucleophilic displacement.

EXPERIMENTAL

Alkyl-aryl transamination. a) A mixture of 3.3 g (0.026 mole) of β-diethylaminopropionitrile, 2.5 g (0.026 mole) of aniline and 3.1 g (0.050 mole) of glacial acetic acid was heated in a flask under reflux for 2 hours at 160° in a metal bath. The mixture was treated with alkali, and the separated oil was extracted with benzene. After removal of the benzene by distillation, two fractions were isolated: aniline with β-phenylaminopropionitrile as impurity, b. p. up to 100° at 5 mm, and β-phenylaminopropionitrile, b. p. 153-155° at 4 mm; yield 1.8 g (56.2 %), m. p. 49° (from alcohol).

b) A mixture of 12.6 g (0.1 mole) of β-diethylaminopropionitrile and 12.95 g (0.1 mole) of aniline hydrochloride was placed in a Claisen flask, fitted with two thermometers (one in the reaction mixture, and the other in the vapors) and a descending condenser. The flask was heated in a metal bath at 180° for 1.5 hours (reaction mixture 160°; vapor temperature 78-82°), at which time 2.2 ml of acrylonitrile distilled off (b. p. 78°, n_D^{20} 1.3930 on redistillation). To the residue in the Claisen flask was added 5.0 g (0.125 mole) of powdered sodium hydroxide, the mixture heated on the boiling water bath, and the diethylamine with aniline impurity distilled off at 56-74° (7.0 ml). The presence of aniline in the distillate was qualitatively shown by testing for primary amine (diazotization and coupling with β-naphthol). After drying over NaOH the mixture was fractionally distilled, the diethylamine distilling at 56° (5.5 ml). Water was added to the residue in the flask, and the obtained oil was extracted

with benzene. After removal of the benzene by distillation the residue was vacuum-distilled. The aniline distilled first (2.9 g), b. p. up to 120° at 20 mm, and then the β-phenylaminopropionitrile with b. p. 178-180° at 10 mm; yield 5.1 g (34.9%, based on taken β-diethylaminopropionitrile); m. p. 49° (from alcohol).

c) A mixture of 3.5 g (0.025 mole) of β-diethylaminopropionitrile and 3.25 g (0.025 mole) of aniline hydrochloride was heated in water (5 ml) at the boil. After the usual treatment we isolated from the reaction mixture: aniline with β-phenylaminopropionitrile as impurity, b. p. up to 110° at 24 mm (1.0 g), and β-phenylaminopropionitrile with b. p. 196° at 24 mm; yield of the latter 1.9 g (52 %), m. p. 50° (from alcohol).

Addition of aniline hydrochloride to acrylonitrile. a) In anhydrous medium. A mixture of 6.5 g (0.050 mole) of aniline hydrochloride and 5.3 g (0.1 mole) of acrylonitrile was heated at the boil for 14 hours. The mixture was treated with dilute caustic solution, and the obtained oil was extracted with benzene. After distilling off the benzene we isolated 2.8 g of aniline, b. p. up to 100° at 4 mm. No residue was left in the flask.

b) In water medium. A mixture of 13.0 g (0.1 mole) of aniline hydrochloride and 5.5 g (0.105 mole) of acrylonitrile in 25 ml of water was heated at the boil for 14.5 hours. After the usual treatment we obtained 7.0 g of aniline and 1.6 g (11%) of β-phenylaminopropionitrile with b. p. 153° at 3 mm and m. p. 49° (from aqueous alcohol).

Conditions for the formation and decomposition of β-diethylaminopropionitrile. Differing from the known conditions for the addition of free diethylamine to acrylonitrile [9, 10], we were able to add both diethylamine hydrochloride and the acetate to acrylonitrile.

a) A mixture of 7.3 g (0.1 mole) of diethylamine, 8.0 g (0.15 mole) of acrylonitrile and 6.0 g (0.1 mole) of glacial acetic acid was heated for 3 hours at the boil. After vacuum-distillation of the volatile products on the water bath and the usual treatment of the residue we obtained 7.4 g (58.7%) of β-diethylaminopropionitrile with b. p. 95-97° at 21 mm.

b) A mixture of 5.5 g (0.05 mole) of diethylamine hydrochloride and 5.3 g (0.1 mole) of acrylonitrile was heated at the boil for 10 hours. We obtained 2.5 g (39.6%) of β-diethylaminopropionitrile with b. p. 92-93° at 18 mm.

c) A solution of 5.5 g (0.05 mole) of diethylamine hydrochloride in 5 ml of water and 3.0 g (0.056 mole) of acrylonitrile was heated at the boil for 14 hours. We obtained 1.5 g (23.8%) of β-diethylaminopropionitrile with b. p. 110-112° at 42 mm.

Decomposition of dry β-diethylaminopropionitrile hydrochloride with removal of volatile products by distillation. The yield of distilled acrylonitrile under the indicated conditions (160-190°) was 77% [1].

Decomposition of aqueous solution of β-diethylaminopropionitrile hydrochloride. A solution of 8.1 g (0.05 mole) of β-diethylaminopropionitrile in 5 ml of water was heated in a Claisen flask with slow removal of water by distillation. Water was added to the mixture during distillation at such a rate that the concentration of the solution remained constant. A total of 20 ml of water was added, while the amount distilled off was 18 ml. The amount of acrylonitrile (b. p. 76°) removed with the water was 1.5 ml. The residue in the flask after evaporation to dryness was treated with 2 g of powdered NaOH. The mixture was heated on the water bath, and here 3.0 ml (2.1 g, 58.3%) of diethylamine with b. p. 56° was collected by distillation.

SUMMARY

1. The mechanism of our discovered [1] reaction of alkyl-aryl transamination in the β-dialkylaminopropionitrile series consists of the cleavage of the dialkylamino radical from the latter, followed by addition of the arylamine to the formed acrylonitrile in the presence of a proton.

2. The opinion held by some authors [4] that the indicated reaction is one of direct nucleophilic displacement of the dialkylamino group by the arylamine radical stands in contradiction to our experimentally established cleavage of acrylonitrile (47%) under the conditions of this reaction, and also to the cleavage of the latter in an amount of 77% when diethylaminopropionitrile hydrochloride is heated in the absence of aniline.

3. The statement made by the same authors that it is necessary to have diethylamine present in order for aromatic amine hydrohalides to add to acrylonitrile is not correct, since the indicated addition does take place in the absence of diethylamine, under the influence of acid catalysts.

LITERATURE CITED

[1] A. F. Bekhli, J. Gen. Chem. 21, 86 (1951). *

[2] L. Bauer, J. Cymerman and W. J. Sheldon, J. Chem. Soc. 1951, 3311.

[3] I. M. Chirkov, M. I. Vinnik, and others, Problems of Chemical Kinetics, Catalysis and Reactivity [in Russian] (Izd. AN SSSR, 1955), p. 496.

[4] J. Cymerman-Craig, M. Moyle, A. J. C. Nicholson and R. L. Werner, J. Chem. Soc. 1955, 3628.

[5] R. J. Bates, J. Cymerman-Craig, M. Moyle and R. J. Young, J. Chem. Soc. 1956, 388.

[6] C. K. Ingold, Structure and Mechanism in Organic Chemistry, N. Y. (1953).

[7] A. F. Bekhli, J. Gen. Chem. 19, 1553 (1949). *

[8] Organic Reactions [Russian translation], Vol. VII, p. 146 (1956).

[9] J. Burckhalter, E. Jones, W. Holcomb and L. Sweet, J. Am. Chem. Soc. 65, 2012 (1943).

[10] A. P. Terent'ev and A. N. Kost, J. Gen. Chem. 16, 859 (1946).

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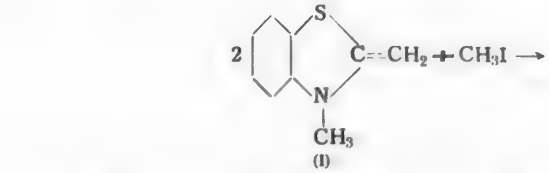
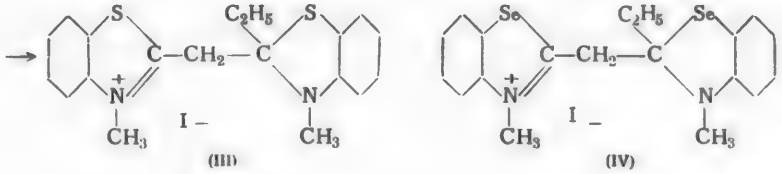
ON THE PRODUCTS OF REACTION BETWEEN METHYLENE BASES OF BENZOTHIAZOLE AND BENZSELENAZOLE AND ALKYL HALIDES

F. S. Babichev and A. I. Kiprianov

Towards the end of 1955 was published the abstract of a patent by Larive and Collet [1] in which the authors described adducts of methyl iodide to 3-methyl-2-methylenebenzthiazoline (I) and 3-methyl-2-methylenebenzselenazoline (II), and the novel triple nuclear dyes obtained from these products. According to Larive and Collet the action of methyl iodide on compound (I) gives rise to the formation of the salt (III).



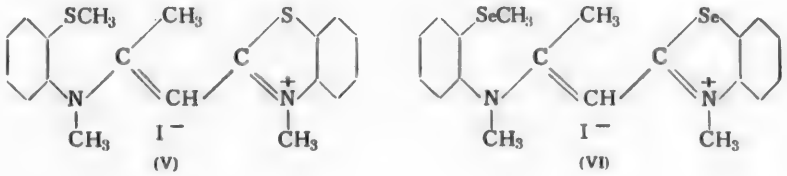
(I)



(III) (IV)

Similarly, from methyl iodide and compound (II) is obtained the corresponding derivative of benzselenazole (IV).

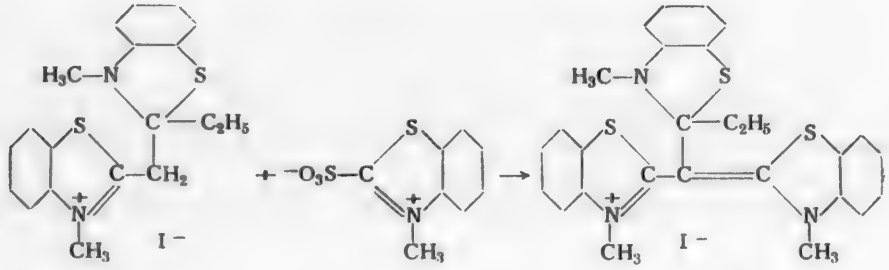
It must be noted, however, that the reaction of methylene bases derived from benzothiazole, benzselenazole and thiazole with alkyl halides has been investigated by us in detail as far back as 1950 [2], and that the structure assigned to these products by Larive and Collet is incorrect. In fact, the reaction of methyl iodide with 3-methyl-2-methylenebenzthiazoline results in the formation of compound (V), while the reaction with 3-methyl-2-methylenbenzselenazoline gives compound (VI).



(V) (VI)

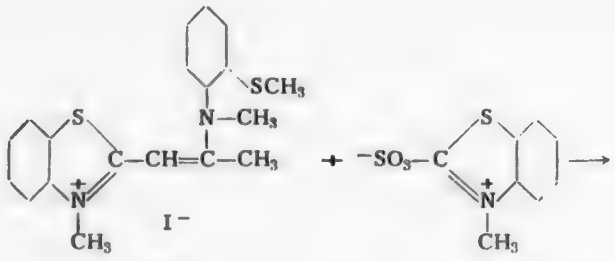
Structures of compounds (V) and (VI) have been confirmed by investigation of their properties and of those of the products of their hydrolysis. Compounds of similar structures have been prepared by Babichev by the interaction of methylene bases derived from benzothiazole with α-haloketones, esters of α-haloacids, halogen substituted acid anhydrides and cyanogen bromide [3].

Larive and Collet have utilized the adducts of methyl iodide to methylene bases in the synthesis of triple-nuclear monomethinecyanines, allegedly through the intermediate stage of the formation of N-methyl-2-benzothiazolesulfobetaine [4]. Having assigned an incorrect structure to the starting materials the authors have, quite naturally, also assigned an incorrect structure to the dyes obtained. According to Larive and Collet, the formation of these dyes proceeds according to the following scheme (taking the benzothiazole derivative as example):

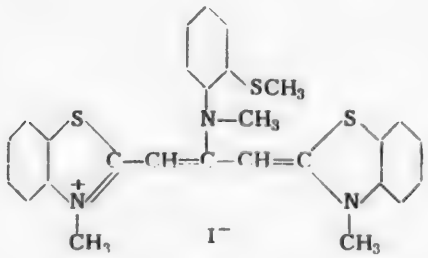


(III) (VII)

In reality, however, the reaction follows an entirely different path, the resultant product being not a monomethinecyanine, as supposed by Larive and Collet, but a trimethine dye substituted in the chain (VIII):



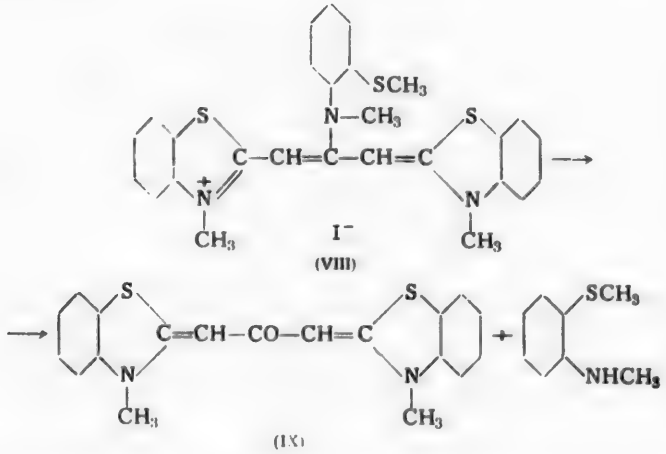
(V)



(VIII)

The reaction between compound (V) and 3-methyl-2-benzthiazolesulfobetaine has been investigated by us in some detail. The orange-colored dye – the product of this reaction – is easily hydrolyzed on heating

with caustic potash. As a result there is formed a yellow-colored substance which melts at 339° with decomposition and which was found to be identical with the authentic ketone (IX) [5] (see below). This ketone has been prepared by us and did not depress the melting point in mixture with the product of hydrolysis. The second compound isolated from the hydrolysate was the methyl ether of o-methylaminothiophenol. The hydrolysis of the dye obtained by Larive and Collet proceeds, therefore, according to the following equation:

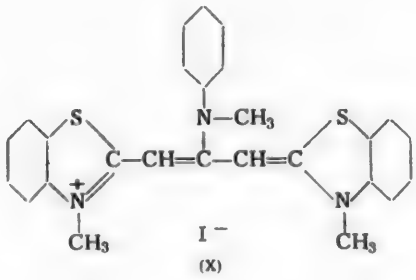


(VIII)

(IX)

These compounds cannot, obviously, be obtained on hydrolysis of a dye having the structure (VII).

Thiocarbocyanines with arylamino groups in the meso position of the chain are well known [6] and resemble in properties compound (VIII). The absorption peak of the dye (VIII) in alcoholic solution lies at 493 mμ, while the absorption maximum of the dyestuff (X), similar in structure to compound (VIII), lies at 497 mμ.



(X)

EXPERIMENTAL

3,3'-Dimethyl-9-[(o-methylmercapto-N-methyl)-phenylamino]-thiocarbocyanine iodide (VIII). A mixture of 4.68 g of the adduct of methyl iodide to 3-methyl-2-methylenebenzthiazoline (I) [7], 3.6 g of N-methyl-2-benzthiazolesulfobetaine [1, 4] and 1.2 g of triethylamine in 30 ml of absolute alcohol was refluxed on a water bath for 1 hour. Subsequently, 60 ml of ether was added to the reaction mixture. The crystals which separated within 24 hours were filtered off, washed with ether and recrystallized from 140 ml of 50% methanol. Yield of the dye after two recrystallizations, 1.85 g (30%). Reddish-orange crystals, m. p. 247° with decomposition (uncorr.); absorption peaks in alcohol at 399 and 493 mμ.

Found %: N 6.82, 6.69; I 20.96, 20.88. $C_{27}H_{28}N_3S_3I$. Calculated %: N 6.83; I 20.61.

Two g of the pure dye was heated for 40 minutes with a solution of 0.5 g of caustic potash in 5 ml of water and 40 ml of alcohol. There separated large yellow needles. After cooling the suspension, the crystals were filtered off, and washed with alcohol, water, followed by a second washing with alcohol and finally with ether. There was obtained 0.65 g of a yellow-colored substance melting at 339° with decomposition (corr.). After a second recrystallization the melting point did not change. Mixture of the substance with 1,3-bis-(3'-methyl-benzothiazolinylidene-2')-propanone (IX), prepared according to Kendall [5], did not depress the melting point. To the mother liquor was added 1 ml of conc. hydrochloric acid. The yellow crystals which separated were filtered off, heated with 5 ml of pyridine, again filtered and washed with ether. Another 0.2 g of the substance was obtained, m. p. 338°, with decomposition. Thus, the total yield of ketone (IX) was 0.85 g (87%).

After removing the alcohol from the mother liquor, 8 ml of water was added to the residue, after which the solution was refluxed for a short period with animal charcoal. After filtering and cooling, sodium hydroxide solution was added to alkaline reaction. The oil which separated was extracted with ether and the ether extract dried over potassium hydroxide. After removing the ether there remained 0.35 g of a yellow oil. On acting on the latter with acetyl chloride in benzene there formed the acetyl derivative of o-methylmercapto-N-methylaniline as long colorless needles, m. p. 81-82° [7]. Mixture of the substance with an authentic sample obtained from N-methylaminothiophenol did not depress the melting point.

SUMMARY

The structure which Larive and Collet have assigned to the adducts of methyl iodide to 3-methyl-2-methylenebenzthiazoline and 3-methyl-2-methylenebenzselenazoline have been found to be incorrect. Likewise, incorrect structures have been assigned to the dyes obtained from these compounds. In the present investigation the true structure of these dyes has been established.

LITERATURE CITED

[1] U. S. Patent 2708669; Ch. A. 49, 15579 (1955).

[2] A. I. Kiprianov and F. S. Babichev, J. Gen. Chem. 20, 145 (1950);* F. S. Babichev, A. M. Matyushinets and D. F. Mironova, Ukr. Chem. J. 19, 405 (1953); F. S. Babichev and L. I. Kravchenko, Ukr. Chem. J. 16, 199 (1950).

[3] F. S. Babichev, J. Gen. Chem. 20, 1904 (1950).*

[4] H. Larive, P. Collet and R. Dennilauler, Bull. Soc. Chim. 1956, 1443.

[5] Brit. Patent, 681, 390; Chem. Ztrbl. 1955, 7130.

[6] N. N. Sveshnikov, I. I. Levkoev, B. S. Portnaia and E. B. Lifshits, Proc. Acad. Sci. USSR, 84, 733 (1952).

[7] A. I. Kiprianov and F. S. Babichev, J. Gen. Chem. 20, 151 (1950).*

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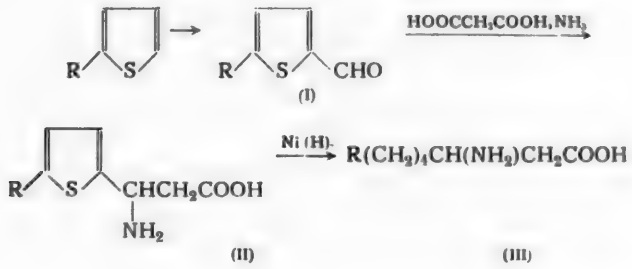
SYNTHESIS OF ALIPHATIC AMINO ACIDS FROM THIOPHENE DERIVATIVES

II. SYNTHESIS OF β-AMINO ACIDS

Ia. L. Gol'dfarb, B. P. Fabrichnyi and I. F. Shalavina

In recent years new data have been published in the literature which indicate that β-amino acids play a more significant role as biologically active compounds than has been hitherto supposed. In addition to the well-known derivatives of β-alanine – the dipeptides: anserine, carnosine, and the very important growth promotor, pantothenic acid – we may mention here a number of antibiotics having a polypeptide structure such as streptotricin, streptolin, viomycin, roseotricin and geomycin; the hydrolysates of all the latter compounds contain β-lysine [1, 2] (β,ε-diamino caproic acid). In addition, α, β-diamino propionic acid has been detected in the acid hydrolysate of viomycin. Recently, β-alanine has been found in co-enzyme "A" and, in the form of glutaminyl-β-alanine cyanide [3], in sweet pea seeds. Similar facts lie at the root of the increased interest which has been accorded β-amino acids and their transformations as, for example, reactions which lead to the formation of dipeptides [2]; parallel with this endeavors have been made to find new ways of synthesizing these amino acids. In this latter respect great possibilities are presented through the use of thiophene and its homologs as the starting materials (cf. [4], 5]).

The path leading from thiophene and its homologs to β-amino acids may be represented by the following scheme:

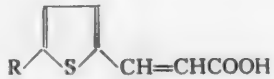


The second stage of this process consists of the condensation of the aldehyde (I) with malonic acid and ammonia to give the β-amino acid according to the well-known method developed by V. M. Rodionov and co-workers [6, 8] a β-amino acid containing thiophene was first synthesized by the method of Mamaev, Suvorov and Rokhlin [9]. The final stage of the reaction is reduction and desulfurization* in the presence of Raney nickel under conditions described earlier [4, 5]. The preparation of β-amino acids by this method affords all the possible synthetic variants already discussed in our recent communications [4, 5] dealing with the synthesis of amino acids of other types, namely, chain lengthening and preparation of amino acids with branched chains.

It will be seen from the scheme shown above that an amino acid with a branched structure will result if the alkyl substituent or aldehydic group are in positions 3 or 4, as also when the substituent in position 5 has a branched structure.

*For brevity's sake this stage of the process will be referred to as hydrogenolysis.

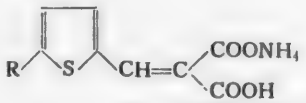
Putting our program of investigation into effect we have, starting from 2-thiophenaldehyde (I, R = H), 5-methyl-2-thiophenaldehyde (I, R = CH_3), 5-ethyl-2-thiophenaldehyde (I, R = C_2H_5) and 5-tert-butyl-2-thiophenaldehyde (I, R = tert-C_4H_9), prepared β-(2-thienyl)-β-aminopropionic (II, R = H), β-(5-methyl-2-thienyl)-β-aminopropionic (II, R = CH_3), β-(5-ethyl-2-thienyl)-β-aminopropionic (II, R = C_2H_5), and β-(5-tert.-butyl-2-thienyl)-β-aminopropionic (II R = tert.-C_4H_9) acids in yields varying from 25 to 41%. The last three acids have not been described previously. The acids have been characterized also in the form of their various derivatives.



(IV)

Unsaturated acids having the structure (IV) have been obtained as by-products namely: β-(2-thienyl)-acrylic acid (IV, R = H), β-(5-methyl-2-thienyl)acrylic acid (IV, R = CH_3), β-(5-ethyl-2-thienyl)acrylic acid (IV, R = C_2H_5) and β-(5-tert-butyl-2-thienyl)acrylic acid (IV, R = tert-C_4H_9). As is well-known, synthesis of amino acids under conditions of the Rodionov reaction is usually accompanied by the formation of the corresponding unsaturated acids (see, for example [9]).

On reducing the reaction time in the case of the preparation of β-(5-methyl-2-thienyl)-β-aminopropionic and β-(5-ethyl-2-thienyl)-β-aminopropionic acids we have, instead of the expected β-amino acids, obtained in good yield the acid ammonium salts of (5-methyl-2-thienyl)methylenemalonic acid (V) and (5-ethyl-2-thienyl)methylenemalonic acid (VI).



(V) R=CH_3; (VI) R=C_2H_5.

These salts may represent the intermediate products of the reaction since on being heated with ammonium acetate they give rise to the formation of the corresponding β-amino acids.

In synthesizing β-(5-tert-butyl-2-thienyl)-β-aminopropionic acid we have come across some unexpected features. The refractive index of 5-tert-butyl-2-thiophenaldehyde (n_D^{20} 1.5462, n_D^{22} 1.5451, n_D^{26} 1.5436) obtained from 2-tert-butyl-thiophene which we prepared by the method described by Sy, Buu-Hoi and Xuong [10] differed from the value given by the latter authors (n_D^{22} 1.5495), but was close to other data published (n_D^{26} 1.5428 [11], n_D^{26} 1.5441 [12]). In addition, the melting point (216-217°) of the semicarbazone of our aldehyde was close to that given by Messina and Brown [13] (215-216°), but differed greatly from the melting point (249°) of the semicarbazone obtained by Buu-Hoi and co-workers [10]. Similarly, the melting point (118-119°) of the oxime of our aldehyde differed from that given by Buu-Hoi [10] for this derivative, but was almost identical with the melting point (121-122°) of the oxime obtained by one of us in collaboration with Antik and Konstantinov [14]. In order to explain the cause of this discrepancy in the melting point of the oxime we decided to alter the conditions of its preparation, but retaining the alkaline pH of the solution. The oxime obtained in this way had a melting point of 73-74° and is probably the geometrical isomer of the oxime with a melting point of 118-119°. Buu-Hoi and co-workers do not describe the conditions of preparation of the oxime melting at 86°. It may well be that the oxime obtained by them is a mixture of the geometrical isomers.

Hydrogenolysis of the thiophene-derived β-amino acids described above was effected by heating them with Raney nickel in the presence of dilute aqueous ammonia. In this way β-amino-n-enantoic acid (III, R = H) was obtained from β-(2-thienyl)-β-aminopropionic acid (II, R = H); the yield of the crude product amounted to about 80%. β-Amino-n.caproic acid (III, R = CH_3) was obtained in lower yield; the yield of β-amino-n.-pelargonic acid was very small, while attempts to prepare ϑ,ϑ-dimethyl-β-aminopelargonic acid (III, R = = tert-C_4H_9) by hydrogenolysis of β-(5-tert-butyl-2-thienyl)-β-aminopropionic acid (II, R = tert-C_4H_9) failed. The situation did, however, change radically when hydrogenolysis was carried out on the acetyl derivatives of the thiophene-substituted β-amino acids instead of on the free acids themselves. By this method the acetyl derivatives of the corresponding aliphatic β-amino acids were obtained in good yields. From the acetyl

derivative of β-(5-ethyl-2-thienyl-β-aminopropionic acid we obtained the acetyl derivative of β-amino-n.-pelargonic acid in a yield of about 78%, while the acetyl derivative of β-(5-tert-butyl-2-thienyl)-β-aminopropionic acid gave the corresponding derivative of 9-dimethyl-β-aminopelargonic acid (yield 55%). On heating the latter with hydrochloric acid we obtained, in over 90% yield, the hydrochloride of 9-dimethyl-β-aminopelargonic acid, and on neutralizing this with alkali – the free amino acid. In carrying out hydrogenolysis of the amino acids their acetyl derivatives should be used in preference to the free acids, because in this way foaming during the reaction is reduced considerably; in addition, the extraction of the product of hydrogenolysis is made easier since the spent nickel catalyst may be dissolved in acid and the acetyl derivative extracted from the acid solution with a suitable solvent.

EXPERIMENTAL

β-(2-Thienyl)-β-aminopropionic acid (II, R = H). From 46.2 g of 2-thiophenaldehyde, 46.0 g of malonic acid (for preparation see [15]) and 131 g of ammonium acetate there was obtained 31.4 g of crude β-(2-thienyl)-β-aminopropionic acid (yield 41.2%, m. p. 201-203°) and 13.3 g of β-(2-thienyl)acrylic acid (IV, R = H). After one recrystallization from dilute alcohol the amino acid melted at 210-211° with decomposition (in a pre-heated melting point apparatus) (literature, 207-208° [9]).

After crystallization from dilute (1 : 1) hydrochloric acid the hydrochloride of this amino acid melted at 170-171° (decomp.) (literature, m. p. 169-171° [9]).

The p-toluenesulfonyl derivative of the acid was obtained by the action of p-toluenesulfonyl chloride on a solution of the acid in 10% sodium carbonate, followed by acidification of this solution. After two recrystallizations from dilute alcohol the compound melted at 160°.

Found %: N 4.40, 4.60. $C_{14}H_{15}O_4NS_2$. Calculated %: N 4.31.

β-(5-Methyl-2-thienyl)-β-aminopropionic acid (II, R = CH_3). To 32.2 g of 5-methyl-2-thiophenaldehyde was added 30.5 g of malonic acid, 49.0 g of ammonium acetate and 100 ml of 96% alcohol. The mixture was heated under reflux on a boiling water bath for 6 hours. At the end of this period 49.0 g of ammonium acetate and 50 ml of 96% alcohol were added, after which the mixture was heated for another six hours. The crystals which separated after prolonged cooling were filtered off and washed with alcohol and ether. There was obtained 10.45 g of the crude amino acid, m. p. 205-206° (decomp.). The filtrate was combined with the alcohol washings and the solution was reduced under vacuum to a volume of 200 ml. To the residue was added 30.0 g of ammonium acetate. The mixture was heated for 6 hours on a boiling water bath. On cooling no precipitate formed. The alcohol and part of the ammonium acetate were removed in vacuo and 400 ml of water was added to the residue. β-(5-Methyl-2-thienyl)acrylic acid (IV, R = CH_3) separated as an oil which was extracted with ether. The aqueous layer was separated and freed from ether by blowing air through it. The solution was then neutralized with sodium hydroxide to weakly acid reaction to litmus, after which a saturated solution of cupric acetate was added. This precipitated the copper salt of β-(5-methyl-2-thienyl)-β-aminopropionic acid. The dry salt weighed 9.48 g. On decomposing this salt with hydrogen sulfide there was obtained 5.3 g of the free amino acid (II, R = CH_3). The total yield of the amino acid was, thus, 15.7 g (33%). After recrystallization from boiling water the amino acid melted at 208° with decomposition.

Found %: C 51.97, 51.85; H 5.94, 5.89; S 17.02, 16.97. $C_8H_{11}O_2NS$. Calculated %: C 51.87; H 5.99; S 17.31.

The hydrochloride was obtained by dissolving the amino acid in concentrated hydrochloric acid and evaporating the solution. After recrystallization from conc. hydrochloric acid it melted at 209-210° with decomposition.

Found %: C 43.16, 43.30; H 5.32, 5.51; Cl 15.96, 15.70. $C_8H_{12}O_2NClS$. Calculated %: C 43.14; H 5.43; Cl 15.92.*

The acetyl derivative was obtained in the following way. 0.6 g of the amino acid was dissolved in 10 ml of 6% sodium hydroxide solution and to the cooled solution was added 1 ml of acetic anhydride. The

* In all hydrochlorides of the amino acids chloride content was determined by the Volhard method.

mixture was shaken for one hour and was then acidified with hydrochloric acid (Congo red). There separated colorless crystals (0.64 g, m. p. 140-142°). After recrystallization from dilute alcohol the compound was obtained in the form of long needles, m. p. 143-144°.

Found %: C 52.63, 52.70; H 5.79, 5.71; S 14.16, 14.23; N 6.04, 5.97. $C_{10}H_{13}O_3NS$. Calculated %: C 52.85; H 5.76; S 14.10; N 6.16.

β-(5-Methyl-2-thienyl)acrylic acid (IV, R = CH_3). The ether extract obtained in the preparation of β-(5-methyl-2-thienyl)-β-aminopropionic acid (see above) was washed with 10% sodium carbonate solution (two 100 ml portions). The soda extract was acidified with concentrated hydrochloric acid to Congo red. There separated a yellow oil which crystallized rapidly. There was obtained 6.54 g of impure unsaturated acid melting at 156-160°. After two recrystallizations from dilute alcohol the acid melted at 164-165°. Literature, m. p. 165-166° [16].

Found %: C 57.05, 57.06; H 4.88, 4.95; S 18.81, 18.71. $C_8H_8O_2S$. Calculated %: C 57.12; H 4.79; S 19.06.

Acid ammonium (5-methyl-2-thienyl)-methylenemalonate (V). To a mixture of 17.2 g of 5-methyl-2-thiophenaldehyde, 15.8 g of malonic acid and 21.0 g of ammonium acetate was added 125 ml of 96% alcohol. The mixture was heated under reflux for 4 hours on a boiling water bath. On cooling the entire contents crystallized. The crystals were filtered off and washed with alcohol and ether. The dry substance weighed 25.2 g. After two recrystallizations from dilute alcohol yellow leaflets were obtained which melted at 182°.

Found %: C 46.93, 47.18; H 4.77, 4.88; N 6.14, 6.13. $C_9H_{11}O_4NS$. Calculated %: C 47.15; H 4.84; N 6.11.

On addition of sodium hydroxide to the aqueous solution of the compound there evolved ammonia gas. On heating 15.0 g of this acid ammonium salt with 30 g of ammonium acetate in 100 ml of alcohol (for 18 hours on a boiling water bath) there was obtained 2.8 g of β-(5-methyl-2-thienyl)-β-aminopropionic acid, m. p. 208°.

β-(5-Ethyl-2-thienyl)-β-aminopropionic acid (II, R = C_2H_5). A mixture of 33.5 g of 5-ethyl-2-thiophenaldehyde, 27.4 g of malonic acid, and 33.5 g of ammonium acetate in 100 ml of 96% alcohol was heated under reflux for 6 hours on a boiling water bath, after which another 33.5 g of ammonium acetate was added and heating continued for a further 6 hours. On prolonged cooling of the reaction mixture in ice there separated a crystalline precipitate. This was filtered off and washed several times with alcohol (the alcoholic washings being collected separately), followed by washing with ether. The dry amino acid weighed 11.4 g, m. p. 203° (decomp.). The filtrate obtained after separating the amino acid, was heated for 6 hours. On cooling in ice, there separated an additional quantity of the amino acid (3.08 g, m. p. 200-201°). In this way, 14.5 g of the impure amino acid (30.5%) was obtained in all. From the filtrate obtained from the isolation of the amino acid, there was extracted β-(5-ethyl-2-thienyl)acrylic acid (see below). After two recrystallizations from boiling water the amino acid melted, in preheated melting point apparatus, at 203-204° with decomposition.

Found %: C 54.00, 54.10; H 6.45, 6.54; N 6.79, 7.01. $C_9H_{13}O_2NS$. Calculated %: C 54.24; H 6.57; N 7.03.

After recrystallization from dilute (1:1) hydrochloric acid the hydrochloride of the amino acid melted at 170-171° with decomposition.

Found %: C 45.67, 45.55; H 5.51, 5.89; Cl 15.01, 14.81. $C_9H_{14}O_2NClS$. Calculated %: C 45.86; H 5.99; Cl 15.05.

The p-toluenesulfonyl derivative melted, after recrystallization from dilute alcohol at 127-128°.

Found %: N 3.99, 4.04. $C_{16}H_{19}O_4NS_2$. Calculated %: N 3.96.

The acetyl derivative was obtained from 5.0 g of the amino acid dissolved in 80 ml of 6% sodium hydroxide solution, and 8.0 ml of acetic anhydride. In all, there was obtained 5.3 g of the acetyl derivative of β-(5-ethyl-2-thienyl)-β-aminopropionic acid, m. p. 128-130°. After recrystallizing the substance from dilute alcohol its melting point was 129-130°.

Found %: C 55.11; H 6.21; S 13.35. $C_{11}H_{15}O_3NS$. Calculated %: C 54.75; H 6.28; S 13.29.

β-(5-Ethyl-2-thienyl)acrylic acid (IV, R = C_2H_5). From the filtrates obtained in the preparation of β-(5-ethyl-2-thienyl)-β-aminopropionic acid (see above), was isolated 11.7 g of an impure unsaturated acid melting at 87-90°. After two recrystallizations of 1.9 g of the impure acid from dilute alcohol there was obtained 0.75 g of a compound melting at 100-101° (literature m. p. 102-103° [16]).

Found %: C 59.33. 59.43; H 5.55, 5.58. $C_9H_{10}O_2S$. Calculated %: C 59.26; H 5.53.

(5-Ethyl-2-thienyl)methylenemalonic acid. A mixture of 26.6 g of 5-ethyl-2-thiophenaldehyde, 23.8 g of malonic acid, 29.4 g of ammonium acetate and 100 ml of 96% alcohol was refluxed for five hours on a boiling water bath. On cooling the reaction mixture crystallized. The acid ammonium salt of acid (VI) which separated was filtered off and washed several times with alcohol and then with ether. There was obtained 26.6 g of a yellow colored substance. After recrystallization from dilute alcohol the salt melted at 168-169°. On addition of caustic soda to a solution of this salt there evolved ammonia. The free acid (VI) was liberated by acidifying an aqueous solution of its ammonium salt with hydrochloric acid. After recrystallization from dilute alcohol the acid had a melting point of 136-137°.

Found %: C 53.28, 53.22; H 4.47, 4.61. $C_{10}H_{10}O_4S$. Calculated %: C 53.08; H 4.45.

Heating the ammonium salt with ammonium acetate in ethyl alcohol resulted in the formation of β-(5-ethyl-2-thienyl)-β-aminopropionic acid, m. p. 200-201°.

2-Tert-butylthiophene was prepared by the method described by Buu-Hoi and co-workers [10]. To a solution of 84 g of thiophene and 111 g of tert-butyl chloride in 1500 ml of anhydrous carbon disulfide was added, with stirring and cooling to 10-12°, 313 g of stannous chloride over a period of one hour. The mixture was stirred at 20° for five hours and was then poured into 5% of ice-cold hydrochloric acid. The carbon disulfide layer was washed with water, sodium carbonate solution, and again with water and was dried over calcium chloride. After removing the carbon disulfide the residue was fractionated (on a 32-plate column). From 84 g of thiophene there was obtained 72 g (51%) of 2-tert-butyl-thiophene, b. p. 161.8-162.8°, n_D^{20} 1.4982 (Literature, b. p. 163-164°, n_D^{20} 1.4987 [17]; b. p. 163.9°, n_D^{20} 1.49788 [18]; b. p. 165°, n_D^{23} 1.5024 [10]).

5-Tert-butyl-2-thiophenaldehyde was obtained by formulating 2-tert-butyl-thiophene [12]. To a mixture of 38 g of N-methylformanilide and 25 ml of phosphorus oxychloride was added dropwise, with stirring, 30 g of 2-tert-butyl-thiophene, the temperature being kept at 35-40° during the addition, after which stirring was continued for another three hours at room temperature. Next day the mixture was poured on 120 g of crushed ice, extracted with ether, the ether extract washed with dilute hydrochloric acid, water, sodium bicarbonate, followed by another washing with water and was finally dried over magnesium sulfate. After removing the solvent the residue was distilled in vacuo. There was obtained 35 g (97%) of an aldehyde boiling at 133° at 23 mm Hg, n_D^{20} 1.5462, n_D^{22} 1.5451, n_D^{26} 1.5436 (Literature, b. p. 135-136° 25 mm, n_D^{26} 1.5428 [11]; b. p. 246° n_D^{22} 1.5495 [10]; b. p. 135-136° 25 mm, n_D^{26} 1.5441 [12]).

High-melting 5-tert-butyl-2-thiophenaldoxime. To a solution of 0.80 g of hydroxylamine hydrochloride and 0.60 g of sodium carbonate in 10 ml of water was added 1.53 g of 5-tert-butyl-2-thiophenaldehyde followed by addition of alcohol (15 ml) until the solution cleared. The solution was then heated for 1 hour on a boiling water bath and after cooling was acidified with dilute hydrochloric acid (to Congo red). To the warmed acid solution was added water until the solution became permanently turbid. On cooling in ice there separated the yellow-colored crystalline oxime together with some oil. After several recrystallizations from dilute alcohol the oxime became colorless and melted at 118-119°. Literature [10] gives a melting point of 86° (method of preparation not described). Since the melting point of our oxime differed from that given in the literature, the compound was analyzed.

Found %: C 59.01, 58.80; H 7.26, 7.13; S 17.02, 17.13. $C_9H_{13}ONS$. Calculated %: C 58.98; H 7.15; S 17.49.

Low-melting 5-tert-butyl-2-thiophenaldoxime. To a solution of 0.72 g of hydroxylamine hydrochloride and 0.61 g of sodium carbonate in 10 ml of water was added 1.25 g of 5-tert-butyl-2-thiophenaldehyde followed by addition of alcohol in an amount necessary to produce a clear solution. The solution was refluxed on a boiling water bath for 1 hour, after which it was allowed to cool somewhat and to the warm solution was added water until permanent turbidity had developed. On cooling there separated an oil which crystallized on prolonged standing in the cold. Yield, 0.75 g, m. p. 72-74°. After two recrystallizations from dilute alcohol the oxime melted at 73-74°.

Found %: C 59.05, 58.57; H 7.45, 7.48; S 17.55, 17.78. $C_9H_{13}ONS$. Calculated %: C 58.98; H 7.15; S 17.49.

β-(5-Tert-butyl-2-thienyl)-β-aminopropionic acid (II, R = tert-C_4H_9). A mixture of 36.3 g of 5-tert.-butyl-2-thiophenaldehyde, 26.5 g of malonic acid 33.5 g of ammonium acetate and 190 ml of 96% alcohol was heated on a boiling water bath for six hours after which another 33.5 g of ammonium acetate was added and heating continued for a further six hours. After prolonged cooling there separated crystals of the amino acid (12.3 g) having a melting point of 193-195°. After recrystallization from water the acid melted at 213° with decomposition.

Found %: C 58.01, 58.03; H 7.59, 7.38; S 14.25, 14.04; N 6.19, 6.01. $C_{11}H_{17}O_2NS$. Calculated %: C 58.12; H 7.54; S 14.11; N 6.16.

The acetyl derivative obtained from 12.3 g of the amino acid dissolved in 250 ml of 10% sodium carbonate solution warmed to 45°, and 25 ml of acetic anhydride. After acidifying the solution there was obtained 10.8 g of the acetyl derivative. After several recrystallizations from dilute methanol and dilute dioxan the compound melted at 105-106°.

Found %: N 4.90, 5.04. $C_{13}H_{19}O_2NS$. Calculated %: N 5.22.

β-(5-Tert-butyl-2-thienyl)-acrylic (IV, R = tert-C_4H_9). The mother liquor obtained after separation of the foregoing aminopropionic acids, was treated as described in the case of the isolation of β-(5-methyl-2-thienyl)acrylic acid. There was obtained 27.1 g of the crude unsaturated acid having yellowish color. After several recrystallizations from dilute alcohol the acid melted at 140°. The pure acid has a pale yellow color.

Found %: C 62.75, 62.81; H 6.67, 6.52; S 15.11, 15.34. $C_{11}H_{14}O_2S$. Calculated %: C 62.82; H 6.71; S 15.24.

β-Amino-n-enantoic acid (III, R = H). To a solution of 10.0 g of β-(2-thienyl)-β-aminopropionic acid in 200 ml of water and 50 ml of a concentrated solution of ammonia was added gradually at a temperature of 70°, with stirring, about 75 g of Raney nickel.* (The spontaneous foaming occurred during the addition.) After stirring at 70-75° for six hours the compound still contained sulfur.** After addition of another 15 g of the catalyst and stirring for a further three hours at 70-75° the reaction for sulfur was negative. The nickel catalyst was then filtered off and washed repeatedly with hot water. The combined filtrates were evaporated under reduced pressure to a volume of about 200 ml. The warm residue was filtered off from the aluminum hydroxide which had separated, and was then evaporated to dryness under reduced pressure on a water bath.

*Raney nickel was prepared by the standard method [20], but the passing of hydrogen during the washing of the catalyst from alkali was omitted.

**Sulfur was tested for as follows: 2-3 ml of the solution was filtered from the catalyst and evaporated to dryness in a test tube. To the residue was added a small piece of sodium and the test tube was heated to red heat and then plunged into a beaker containing 5-10 ml of water; the resulting solution was filtered. The appearance of a raspberry color on addition of dilute solution of sodium nitroprusside indicated the presence of sulfur.

The impure amino acid weighed 6.7 g (79 %), m. p. 196-198°. After recrystallization from absolute alcohol (with charcoal) the amino acid melted at 201-202°.

Found %: C 57.74, 58.00; H 10.42, 10.53; N 9.52, 9.69. $C_7H_{15}O_2N$. Calculated %: C 57.90; H 10.41; N 9.65.

The hydrochloride of the amino-enantoic acid was obtained from 2.5 g of the impure acid dissolved in 5 ml of warm concentrated hydrochloric acid. On cooling, crystals of the hydrochloride separated from the solution. After drying in a vacuum dessicator over phosphorus pentoxide the substance weighed 1.34 g. After several recrystallizations from conc. hydrochloric acid the hydrochloride melted at 115-116°.

Found %: C 46.54, 46.43; H 8.78, 8.88; Cl 19.43, 19.41. $C_7H_{16}O_2NCl$. Calculated %: C 46.27; H 8.88; Cl 19.52.

The acetyl derivative was prepared as follows. To a solution of 3.2 g of the amino acid in 80 ml of 6% sodium hydroxide solution, cooled to 0°, was added 6.0 ml of acetic anhydride. After two hours the solution was acidified with hydrochloric acid but no precipitate formed. The solution was then reduced on a water bath to a volume of about 30 ml and was decanted from the salt which separated. On standing in the cold there separated colorless crystals (2.05 g) which after several recrystallizations from hot water melted at 74.5-76°.

Found %: C 57.59, 57.76; H 9.05, 9.20. $C_9H_{17}O_3N$. Calculated %: C 57.73; H 9.14.

The p-toluenesulfonyl derivative of the amino-enantoic acid was obtained by the action of p-toluenesulfonyl chloride on a solution of the amino acid in 10% sodium carbonate solution, followed by acidification of the solution. After recrystallization from dilute alcohol the compound melted at 94-95°.

Found %: C 56.40, 56.22; H 7.00, 7.15; S 10.89, 11.03. $C_{14}H_{21}O_4NS$. Calculated %: C 56.16; H 7.07; S 10.71.

4-n-Butyldehydrouracil. 4.5 g of β-amino-n-enantoic acid, 20.0 g of urea and 50 ml of water were heated on a boiling water bath for 15 hours. The filtered solution was extracted with ether, the aqueous layer was acidified with hydrochloric acid and evaporated to dryness with repeated additions of hydrochloric acid. To the dry residue was added 50 ml of water. The insoluble portion was filtered off and washed with water. The weight of the dry substance was 3.1 g, m. p. 168°. After recrystallization from dilute alcohol the melting point was unaltered.

Found %: C 56.11, 56.15; H 8.26, 8.16; N 16.32, 16.56. $C_8H_{14}O_2N_2$. Calculated %: C 56.45; H 8.29; N 16.46.

β-Amino-n-caprylic acid (III, R = CH_3) was obtained in low yield by hydrogenolysis of β-(5-methyl-2-thienyl)-β-aminopropionic acid carried out as described in the case of the amino-enantoic acid. After recrystallization from alcohol the substance melted at 202-204° (decomp.). Literature [19], m. p. 204-206° (decomp.).

Found %: N 8.48, 8.48. $C_8H_{17}O_2N$. Calculated %: N 8.80.

4-n-Amyldehydrouracil was prepared by heating β-amino-n-caprylic acid with urea followed by evaporation of the solution with hydrochloric acid. After two recrystallizations from dilute alcohol, m. p. 181-182° (literature, m. p. 182-184° [19]).

Found %: C 58.36, 58.55; H 8.64, 8.59; N 15.27, 15.10. $C_9H_{16}O_2N_2$. Calculated %: C 58.65; H 8.76; N 15.22.

β-Amino-n-pelargonic acid (III, R = C_2H_5). Hydrogenolysis of 5.0 g of β-(5-ethyl-2-thienyl)-β-aminopropionic acid yielded only 0.74 g of β-amino-n-pelargonic acid. After recrystallization from hot water the melting point was 205°. Mixture with a specimen of β-amino-pelargonic acid prepared by V. K. Zvorykina [7] melted at 204-205°.

The p-toluenesulfonyl derivative of this amino acid was obtained as an oil which did not crystallize.

4-n-Hexyldehydrouracil was prepared as indicated above by the action of urea on the amino-pelargonic acid. After recrystallization from dilute alcohol the compound melted at 185-186° and did not depress the melting point of an authentic sample prepared from β-amino-n-pelargonic acid by V. K. Zvorykina [7].

The acetyl derivative of β-amino-n-pelargonic acid. To a solution of 9.0 g of the acetyl derivative of β-(5-ethyl-2-thienyl)-β-aminopropionic acid in 200 ml of water and 50 ml of concentrated ammonia solution was added at a temperature of 70°, with stirring, about 45 g of Raney nickel. After stirring for three hours at 70-75° the test for sulfur was negative. The solution was filtered from the nickel catalyst which was subsequently washed several times with hot water. The filtrates were combined and evaporated to dryness under reduced pressure; the residue was dissolved in 50 ml of 6% sodium hydroxide. The resultant solution was filtered from the precipitate of nickel hydroxide, and the filtrate was acidified with hydrochloric acid (Congo red). The crystals which separated were washed with water and dried in a vacuum dessiccator over phosphorus pentoxide and weighed 6.2 g (77.5%), melting at 96-98°. After recrystallization from dilute alcohol substance melted at 99-100.5° and did not depress the melting point in mixture with the acetyl derivative prepared by acetylation of β-amino-n-pelargonic acid.

The acetyl derivative of 9,9-dimethyl-β-amino-n-pelargonic acid. To a solution of 6.0 g of the acetyl derivative of β-(5-tert.butyl-2-thienyl)-β-amino propionic acid in 200 ml of water was added at 70°, 50 ml of concentrated ammonia solution and about 30 g of Raney nickel. Stirring was continued for 6 hours at 70-75°. As the test for sulfur was positive, another 6 g (approx.) of nickel was added and stirring was continued at 70-75° until the test for sulfur was negative (5 hrs.). After separating the nickel catalyst the solution was treated as in the foregoing example. The residue weighed 2.32 g, m. p. 106-108°. The spent nickel catalyst was dissolved with dilute (1:1) hydrochloric acid, the solution was neutralized with alkali to pH 5 and extracted with ether. After removing the ether there remained 0.6 g of a substance melting at 108-109°. Thus the combined yield of the crude acetyl derivative amounted to 2.92 g (55%). After recrystallization from dilute methanol the compound melted at 111-112°.

Found %: C 64.14, 63.90; H 10.21, 10.29; N 5.81, 5.69. $C_{13}H_{25}O_3N$. Calculated %: C 64.16; H 10.36; N 5.76.

The hydrochloride was obtained as follows. 3.82 g of the acetyl derivative of the dimethylamino-pelargonic acid and 50 ml of dilute (1:1) hydrochloric acid was refluxed for 12 hours. On cooling there separated a copious crystalline precipitate. The crystals were filtered off and washed with cold dilute (1:1) hydrochloric acid. After drying in a vacuum dessiccator over phosphorus pentachloride, the hydrochloride weighed 3.14 g, m. p. 185-190°. After two recrystallizations from dilute hydrochloric acid it melted at 195-196° (decomp.).

Found %: C 55.28, 55.51; H 9.92, 9.91; Cl 14.85, 15.19. $C_{11}H_{24}O_2NCl$. Calculated %: C 55.56; H 10.17; Cl 14.91.

9,9-Dimethyl-β-amino-pelargonic acid. 2.12 g of the hydrochloride of this amino acid was dissolved in 20 ml of warm water and to the solution was added 0.36 g of sodium hydroxide; the resultant alkaline solution was acidified (litmus) with acetic acid. On cooling the solution there separated the free amino acids. The dried substance weighed 1.60 g (yield 89%), m. p. 185-187°. After repeated recrystallization from boiling water the amino acid melted at 197-198° with decomposition.

Found %: C 65.37; H 11.39; N 7.02, 6.85. $C_{11}H_{23}O_2N$. Calculated %: C 65.63; H 11.51; N 6.96.

SUMMARY

1. A new method of preparation of aliphatic β-amino acids has been outlined.

2. Following the method developed by V. M. Rodionov, the authors have prepared β-(2-thienyl)-β-aminopropionic acid, β-(5-methyl-2-thienyl)-β-aminopropionic acid, β-(5-ethyl-2-thienyl)-β-aminopropionic acid and β-(5-tert-butyl-2-thienyl)-β-aminopropionic acid, starting from the corresponding substituted 2-thiophenaldehydes.

3. By hydrogenolysis of the above thiophene-substituted amino acids the authors have obtained β-amino-n-enantoic, β-amino-n-caprylic and β-amino-n-pelargonic acid.

4. Hydrogenolysis of the acetyl derivatives of β-(5-ethyl-2-thienyl)-β-aminopropionic and β-(5-tert.-butyl-2-thienyl)-β-aminopropionic acids gave, respectively, the acetyl derivatives of β-amino-n-pelargonic and 9,9-dimethyl-β-amino-n-pelargonic acids.

5. Saponification of the acetyl derivative of 9,9-dimethyl-β-aminopelargonic acid with hydrochloric acid yielded the hydrochloride of 9,9-dimethyl-β-aminopropionic acid; neutralization of the latter gave the free amino acid.

LITERATURE CITED

[1] H. Musso, Angew. Chem. 68, 313 (1956).

[2] L. Birkofer and I. Hartwig, Ber. 89, 1608 (1956).

[3] E. D. Schilling and F. M. Strong, J. Am. Chem. Soc. 77, 2843 (1955).

[4] Ia. L. Gol'dfarb and B. P. Fabrichnyi, Proc. Acad. Sci. USSR, 100, 461 (1955).

[5] Ia. L. Gol'dfarb, B. P. Fabrichnyi and I. F. Shalavina, J. Gen. Chem. 26, 2595 (1956);* Proc. Acad. Sci. USSR, 109, 305 (1956);* Bull. Acad. Sci. USSR, Div. Chem. Sci. (1956), 1276.*

[6] W. Rodionoff, E. Malevinskaja and A. Fedorova, Ber. 59, 2952, (1926); 60, 804 (1927).

[7] V. M. Rodionov and V. K. Zvorykina, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1943, 216.

[8] V. M. Rodionov and V. K. Zvorykina, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1945, 233.

[9] V. P. Mamaev, N. N. Suvorov and E. M. Rokhlin, Proc. Acad. Sci. USSR, 101, 269 (1955).

[10] M. Sy, N. P. Buu-Hoi and N. D. Xuong, J. Chem. Soc. 1954, 1975.

[11] U. S. Patent, 2601479; Ch. A. 47, 2215 (1953).

[12] Ia. L. Gol'dfarb and P. A. Constantinov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1956, 992.*

[13] N. Messina and E. V. Brown, J. Am. Chem. Soc. 74, 920 (1952).

[14] Ia. L. Gol'dfarb, L. V. Antik and P. A. Constantinov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1956, 624.*

[15] V. K. Zvorykina, Ind. Org. Chem. 2, No. 15/16, 175 (1936).

[16] W. J. King and F. F. Nord, J. Org. Ch. 14, 405 (1949).

[17] W. M. Kutz and B. B. Corson, J. Am. Chem. Soc. 68, 1477 (1946).

[18] W. G. Appleby, A. F. Sartor, S. H. Lee and S. W. Kapranos, J. Am. Chem. Soc. 70, 1552 (1948).

[19] K. Lang and F. Adikes, Z. physiol. Ch. 269, 236 (1941).

[20] Organic Syntheses, Foreign Literature Press [Russian translation], 4, 349 (1953).

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SYNTHESIS OF PYRROLIDINE BASES FROM γ-KETOALCOHOLS

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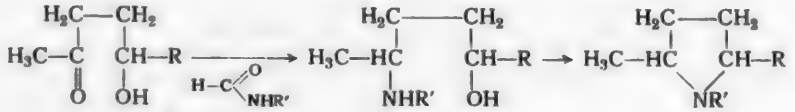
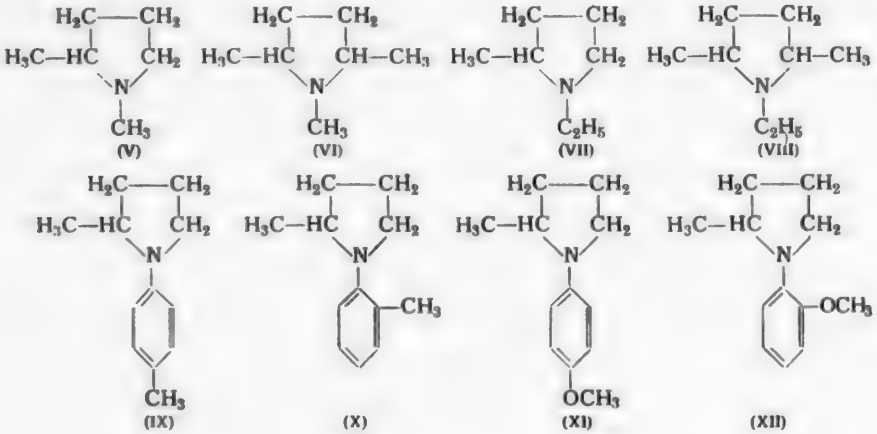
In a preliminary communication we have shown [1] that on heating γ-acetopropyl alcohol and secondary γ-acetobutyl alcohol with formamide and N-phenylformamide in the presence of a nickel catalyst amination and reduction of the carbonyl group takes place, followed by ring closure through the NH_2 and OH groups in positions 1,4. The reaction products were identified as the corresponding pyrrolidine bases, namely, α-methylpyrrolidine (I), 2,5-dimethylpyrrolidine (II), N-phenyl-2-methylpyrrolidine (III) and N-phenyl-2,5-dimethylpyrrolidine (IV).



In the present paper we describe these syntheses in greater detail and we show the possibility of an extension of this reaction.

Continuing our investigation of the hydroamination of γ-acetopropyl and of secondary γ-acetobutyl alcohols we employed different N-substituted derivatives of formamide (N-methylformamide, N-ethylformamide, N-p-tolylformamide, N-o-tolylformamide, N-p-anisylformamide, N-o-anisylformamide). In all cases we obtained the corresponding pyrrolidine bases.



The necessary N-substituted derivatives of formamide were prepared prior to the hydroamination reaction by mixing the corresponding amine with formic acid (to strongly acid reaction to Congo red), followed by distillation from the mixture of water and excess formic acid up to 160° (thermometer in reaction mixture). The N-substituted formamides contained a small amount of residual formic acid.

In all cases the nickel catalyst was found to facilitate lowering of the reaction temperature without appreciably affecting the yields of the pyrrolidine bases which varied from 20 to 50%. In the case of α-methylpyrrolidine we were able to raise the yield to 30% (cf. our previously published data [1]).

In the case of secondary γ-acetobutyl alcohol the yields of the corresponding pyrrolidine bases were always lower and in general did not exceed 30%. This fact would suggest that the presence of substituents in positions 2,5, on the one hand, hinders ring closure, while on the other it renders such a ring unstable under the given reaction conditions. This suggestion finds confirmation in some investigations of transformations of heterocyclic compounds carried out by Iu. K. Iur'ev [2].

EXPERIMENTAL

γ-Acetopropyl alcohol. The material used was technical acetopropyl alcohol (commercial) distilled twice in vacuo.

B. p. 114-115°(30 mm) n_D^{20} 1.4395, d_4^{20} 1.0068, MR_D 26.69. Literature data for acetopropyl alcohol [3]: b. p. 115-116 (30 mm) n_D^{20} 1.4390.

Secondary γ-acetobutyl alcohol was prepared by condensing the sodium derivative of acetoacetic ester with propylene oxide [4]. The condensation was effected without isolating α-aceto-γ-valerolactone whereby it was possible to raise the yield of secondary γ-acetobutyl alcohol to 72%.

B. p. 60-61° (4 mm) n_D^{20} 1.4328, d_4^{20} 0.9634, MR_D 31.31; calc. 31.44. Literature [4]: b. p. 79-82° (16 mm) n_D^{20} 1.4312, d_4^{25} 0.9626.

α-Methylpyrrolidine (I). A mixture of 30.6 g of freshly distilled acetopropyl alcohol, 90 g of formamide and 3 g of nickel catalyst (prepared by ignition of nickel formate) was heated at 110-120° until the evolution of carbon dioxide ceased (10-14 hours). As the evolution of the gas subsided the temperature was gradually raised to 160° (thermometer dipping in the reaction mixture). The reaction product was hydrolyzed by refluxing with 150 ml of concentrated hydrochloric acid for 2-3 hours. After cooling, the reaction mixture was transferred into a three-necked flask provided with a stirrer, reflux condenser and dropping funnel, and was mixed with 50 ml of ether. To the well-stirred and cooled mixture was added, slowly and dropwise, a 40% solution of caustic soda to strongly alkaline reaction. The ether layer was then separated, the aqueous layer was extracted several times with ether, and the combined ether extracts were dried with fused alkali. After removing the ether and distilling the residue twice there was obtained 7.5 g (30%) of α-methylpyrrolidine.

B. p. 97-98.5° at 744 mm; n_D^{20} 1.4340, d_4^{20} 0.8343, MR_D 26.58; calc. 26.69. Literature [5]: b. p. 104-104.5° at 755 mm, n_D^{20} 1.4372, d_4^{20} 0.8307.

The picrate of α-methylpyrrolidine was formed in anhydrous ether, m. p. 88.5-89.50°.

1,2-Dimethylpyrrolidine (V). A mixture of 20.4 g of acetopropyl alcohol, 60 g of methylformamide and 2 g of Ni (from nickel formate) was heated at 110-160° until evolution of carbon dioxide ceased. Hydrolysis was effected by refluxing with 100 ml of concentrated hydrochloric acid. The subsequent treatment was similar to that described above for α-methylpyrrolidine. 5.6 g (28%) of 1,2-dimethylpyrrolidine was obtained.

B. p. 92-94° (747 mm) n_D^{20} 1.4240, d_4^{20} 0.7983, MR_D 31.70; calc. 31.64. Literature [5]: b. p. 96-97° (752 mm) n_D^{20} 1.4252, d_4^{20} 0.7994.

The picrate was formed in alcohol, m. p. 235-236°.

Found %: C 44.03, 44.25; H 4.98, 5.20. $C_{12}H_{16}O_7N_4$. Calculated %: C 43.90; H 4.91.

1,2,5-Trimethylpyrrolidine (VI). Thirteen g of sec-γ-acetobutyl alcohol, 45 g of freshly distilled methylformamide and 1.5 g of Ni was heated at 110-160° until carbon dioxide ceased to evolve. After hydrolysis by refluxing with 60 ml of concentrated hydrochloric acid, 1,2,5-trimethylpyrrolidine was isolated as described in the foregoing preparations. There was obtained 2.5 g (20%) of 1,2,5-trimethylpyrrolidine.

B. p. 111-112° (732 mm) n_D^{20} 1.4260, d_4^{20} 0.7987, MR_D 36.32; calc. 3626. Literature [6]: b. p. 115-116° (750 mm) d_4^{20} 0.8149.

The picrate was formed in alcohol, m. p. 162-164° (decomp.).

Found %: C 45.78, 45.79; H 5.63, 5.33. $C_{13}H_{18}O_7N_4$. Calculated %: C 45.61; H 5.30.

1-Ethyl-2-methylpyrrolidine (VII). On heating 20.4 g of acetopropyl alcohol, 60 g of freshly distilled ethylformamide and 2 g of nickel catalyst, and treating the reaction mixture as described above, there was obtained 11.3 g (50%) of 1-ethyl-2-methylpyrrolidine.

B. p. 117.5-118° (752 mm) n_D^{20} 1.4300, d_4^{20} 0.8052, MR_D 36.31; calc. 36.26. Literature [5]: b. p. 119-120° (754 mm) n_D^{20} 1.4325, d_4^{20} 0.8028.

The picrate was formed in alcohol, m. p. 192-193°.

Found %: C 45.80, 45.70; H 5.49, 5.42. $C_{13}H_{18}O_7N_4$. Calculated %: C 45.61, H 5.30.

1-Ethyl-2,5-dimethylpyrrolidine (VIII). Heating a mixture of 15 g of sec-γ-acetobutyl alcohol, 45 g of freshly distilled ethylformamide and 1.5 g of Ni, followed by the usual treatment, yielded 3.2 g (20.8%) of 1-ethyl-2,5-dimethylpyrrolidine.

B. p. 132-134° (746 mm) n_D^{20} 1.4290, d_4^{20} 0.80524, MR_D 40.66; calc. 40.88. Literature [7]: b. p. 130-131.5°.

The picrate was formed in alcohol, m. p. 192-193°.

Found %: C 46.57, 46.93; H 5.77, 5.61. $C_{14}H_{20}O_7N_4$. Calculated %: C 47.29; H 5.65.

1-p-Tolyl-2-methylpyrrolidine (IX). A mixture of 30.6 g of γ-acetopropyl alcohol, 96 g of freshly distilled formyl-p-toluidine and 3 g of Ni was heated at 110-115° until evolution of carbon dioxide ceased. The reaction mixture (dark viscous liquid, solidifying on cooling) was hydrolyzed by refluxing with 75 ml of concentrated hydrochloric acid for 3 hours. After cooling 40% sodium hydroxide solution was added to the contents of the flask to strongly alkaline reaction. The dark oily layer which separated was removed, the aqueous layer extracted with ether, and the combined extracts were dried with fused alkali. After removing the ether the residue was distilled in vacuo. Excess p-toluidine came over first, followed by 1-p-tolyl-2-methyl pyrrolidine. After two distillations and treatment with benzenesulfonyl chloride there was obtained 31 g (59%) of 1-p-tolyl-2-methylpyrrolodine.

B. p. 133-134° (10 mm) n_D^{20} 1.5580, d_4^{20} 0.9664, MR_D 58.45; calc. 55.76. Literature [2]: b. p. 115° (5 mm) n_D^{20} 1.5572, d_4^{20} 0.9648, MR_D 58.12.

The picrate (formed in alcohol) melts at 128-131°.

Found %: C 53.35, 53.50; H 5.15, 5.13. $C_{18}H_{20}O_7N_4$. Calculated %: C 53.46; H 4.99. Literature [2]: b. p. 115° (5 mm) n_D^{20} 1.5572, d_4^{20} 0.9648; MR_D 58.12.

1-o-Tolyl-2-methylpyrrolidine (X). Heating a mixture of 20.4 g of acetopropyl alcohol, 54 g of formyl-o-toluidine and 1.5 g of Ni, followed by the treatment described for compound (IX), gave 8.3 g (23%) of 1-o-tolyl-2-methylpyrrolidine.

B. p. 100-102° (8 mm) n_D^{20} 1.5405, d_4^{20} 0.9693, MR_D 56.77; calc. 55.75. Literature [2]: b. p. 97-98° (5 mm) n_D^{20} 1.5438, d_4^{20} 0.9725, MR_D 56.79.

The picrate melts at 145-146° (from alcohol).

Found %: C 53.59, 53.69; H 5.07, 5.29. $C_{18}H_{20}O_7N_4$. Calculated %: C 53.46; H 4.99.

1-p-Anisyl-2-methylpyrrolidine (XI). Interaction of 20.4 g of γ-acetopropyl alcohol with 80 g of formyl-p-anisidine in the presence of 1.5 g of Ni, followed by treatment similar to that described above, yielded 11.5 g (40%) of 1-p-anisyl-2-methylpyrrolidine.

B. p. 160° (12 mm) n_D^{20} 1.5625, d_4^{20} 1.0480, MR_D 59.21; calc. 57.40.

The picrate melts at 161-162° (from benzene).

Found %: C 51.99, 51.88; H 4.99, 4.90. $C_{18}H_{20}O_8N_4$. Calculated %: C 51.42; H 4.79.

1-o-Anisyl-2-methylpyrrolidine (XII). Heating 30.6 g of γ-acetopropyl alcohol, 80 g of formyl-o-anisidine and 3 g of Ni gave 19 g (33%) of 1-o-anisyl-2-methylpyrrolidine.

B. p. 127-129° (10 mm) n_D^{20} 1.5570, d_4^{20} 1.0428; MR_D 58.90; calc. 57.40.

The picrate melts at 162-163.5°.

Found %: C 54.18, 54.14; H 5.40, 5.35. $C_{18}H_{20}O_8N_4$. Calculated %: C 51.42; H 4.79.

SUMMARY

1. Hydroamination of γ-acetopropyl and sec-γ-acetobutyl alcohols with formamide and its N-substituted derivatives has been investigated. It has been shown that the reaction gives rise to the formation of the corresponding pyrrolidine bases in yields of 20-50%.

2. The lower yield of pyrrolidine bases obtained from sec-γ-acetobutyl alcohol appears to be due to the instability of the pyrrolidine ring having substituents in positions 2,5.

LITERATURE CITED

[1] A. P. Terent'ev and M. A. Volodina, Proc. Acad. Sci. USSR, 88, 845 (1953).

[2] Iu. K. Iur'ev, J. Gen. Chem. 11, 1129 (1941).

[3] I. L. Knunlants, G. V. Chelintsev and E. D. Osetrova, Proc. Acad. Sci. USSR, 1, 312 (1934).

[4] P. Smith and A. MacDonald, J. Am. Chem. Soc. 72, 1037 (1950).

[5] Iu. A. Iur'ev, J. Gen. Chem. 8, 1934 (1938).

[6] L. Knorr and P. Rabe, Ber. 34, 3500 (1901).

[7] R. A. Robinson, J. Chem. Soc. 16, 1917 (1952).

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HALOARYLATION OF UNSATURATED COMPOUNDS BY AROMATIC DIAZO COMPOUNDS

X. SYNTHESIS OF DL-PHENYLALANINE AND ITS HOMOLOGS

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L-Phenylalanine belongs to the number of the so-called essential amino acids. D-Phenylalanine enters into the composition of the antibiotic gramicidin C. Some of the derivatives of phenylalanine are of significance as biologically active materials. Thus, 3-methyltyrosine, p-fluorophenylalanine, and 2,5-dimethylphenylalanine show a specific inhibiting effect on decarboxylase and in connection with this they lower the blood pressure [1]. p-Nitrophenylalanine is a structural element of the antibiotic Chloromycetin.

In this connection the search for new methods of synthesis of phenylalanine and its derivatives that differ from those described in the literature in their greater simplicity and the availability of the starting materials is of much significance.

Gaudry [2] succeeded in preparing phenylalanine (I) and tyrosine (II), which were contaminated with cinnamic and p-hydroxycinnamic acids, from α-chloro-β-arylpropionitriles in small yields (17-20 %). The reason for the small yields of (I) and (II) was the unfortunate choice of a method of hydrolysis of the chloropropionitriles with concentrated sulfuric or hydrochloric acid. L'Eckyer [3] showed by the example of the hydrolysis of methyl-α-chloro-β-(p-nitrophenyl)isobutyrate that under these conditions splitting out of hydrogen chloride and formation of α-methyl-p-nitrocinnamic acid occurs simultaneously with the hydrolysis of the ester. M. M. Shemiakin and coworkers [4] described the synthesis of (I) and (II) labeled with N^{15} from the corresponding esters of α-bromo-β-phenyl- and α-bromo-β-(p-methoxyphenyl)propionic acids and potassium N^{15} phthalimide. In turn, the ester of bromophenylpropionic acid was prepared from natural phenylalanine. Therefore this method cannot serve for the preparation of phenylalanine derivatives. Moreover, as has been shown in one of our reports [5], of cinnamic acids and phthalimide are formed in high yields by the action of potassium phthalimide on esters of α-halo-β-arylpropionic acids.

Employing the haloarylation of derivatives of acrylic acid [6], we have developed a method [7] for the synthesis of α-halo-β-arylpropionic and β-arylbutyric acids by hydrolysis of the nitriles and esters of these acids with a mixture of formic and hydrochloric acids. This permitted us further to find a general method of synthesis of DL-β-phenylalanine and its derivatives from acrylonitrile and methylmethacrylate.

$$CH_2{=}CHCN \xrightarrow{ArN_2X} ArCH_2\underset{X}{CHCN} \xrightarrow{HCOOH+HCl} ArCH_2\underset{X}{CHCOOH} \xrightarrow{NH_3} ArCH_2\underset{NH_2}{CHCOOH}$$

As a rule aminonitriles are not produced by the direct action of ammonia and amines on α-halo-β-arylpropionitriles. An exception is α-chloro-β-phenylpropionitrile (III), which upon treatment with aniline and subsequent hydrolysis of the aminonitrile by heating with potassium hydroxide yields N,β-diphenylalanine. By heating (III) and α-chloro-β-(p-nitrophenyl)propionitrile (IV) with urotropine in dioxane and subsequent decomposition of the urotropine complex with an alcoholic solution of HCl, the hydrochlorides of the ethyl esters of phenylalanine and p-nitrophenylalanine (V) were obtained in satisfactory yields.

In search of a convenient method for the preparation of amino acids we subjected α-halo-β-arylpropionic acids to amination by one of three methods: by the action of a concentrated aqueous solution of ammonia, by the action of liquid ammonia, and finally, by the action of urotropine. As a result we obtained 50-90% yields of phenylalanine (I), p-methoxyphenylalanine (VI), p-chlorophenylalanine (VII), 2,4-dichlorophenylalanine (VIII), and p-bromophenylalanine (IX). From (VI) we prepared tyrosine (II) in 90% yield. In the synthesis of the acids mentioned, the use of liquid ammonia always gave higher yields than working in aqueous solutions. In addition, the reaction proceeded more rapidly.

Attempts to prepare (V) by direct amination of α-chloro-β-(p-nitrophenyl)propionic acid (X) proved unsuccessful, since in this case p-nitrocinnamic acid always was formed. Amination of (X) with urotropine permitted us to obtain (V) in good yield.

Recently a synthesis has been described for a homolog of (I) – α-methyl-β-phenylalanine (XI) – carried out by a very complex method [8] in 5-6 stages, starting with benzyl cyanide. We prepared (XI) and α-methyl-β-(p-nitrophenyl)alanine, and also their esters, by amination with urotropine of the corresponding α-chloro-β-arylisobutyric acids, for which a means of synthesis has previously been proposed by us [7].

EXPERIMENTAL

Phenylalanine (I) from α-chloro-β-phenylpropionic acid (XII). a) Action of aqueous ammonia solution. 1.5 g of (XII) was heated in a sealed ampoule with 5 ml of 25% ammonia solution and 2 g of ammonium carbonate at 40-50° for 60 hours. After cooling, the ampoule was opened and the contents after 10 hours boiling were evaporated on a water bath to a volume of 1 ml. The solid residue was separated, washed with ice water, and dried. 0.5 g (40%) of phenylalanine was obtained. M. p. 271-272° (with decomp.) after recrystallization from water. By treatment of 0.35 g of (I) with benzoyl chloride (1 ml) in solution at 0°, we obtained N-benzoyl-β-phenylalanine with m. p. 186-187°. A melting point test of a mixture of this product and N-benzoyl-β-phenylalanine from phenylalanine prepared from acetamidomalonic ester and benzoyl chloride [9] gave no depression.

b) Action of liquid ammonia. One g of (XII), 0.5 g of ammonium chloride, and 50 ml of liquid ammonia were placed in an ampoule. After the mixture had stood for 3 days at 20° and had been worked up in the usual manner, 0.37 g of phenylalanine (42%) was obtained with m. p. 272-273° (with decomp.).

Phenylalanine (I) from α-bromo-β-phenylpropionic acid (XIII). a) Action of aqueous ammonia solution. In a bottle with a ground glass stopper were placed 27 g of (XIII) and 250 ml of concentrated ammonia solution, and the mixture was shaken on a rocking device for 7 days at 18-20°. After the usual treatment, 14.5 g of phenylalanine (74%) was obtained with m. p. 271-273° (with decomp.).

b) Action of liquid ammonia. From 2 g of (XIII), 1 g of ammonium chloride, and 50 ml of liquid ammonia at 20° (3 days) we obtained 1.15 g of phenylalanine (80%) with m. p. 273° (with decomp.).

p-Methoxyphenylalanine (VI) from α-chloro-β-(p-methoxyphenyl)propionic acid. From 1.7 g of (XIV), 1 g of ammonium chloride, and 50 ml of liquid ammonia (20°, 3 days) we obtained in the usual way 1.1 g of (VI) with m. p. 291-293° (with decomp.). Yield 70%. Literature data: m. p. 293° (with decomp.) [10].

p-Methoxyphenylalanine from α-bromo-β-(p-methoxyphenyl)propionitrile (XV). 4.4 g of (XV) was heated in a flask with a reflux condenser to 100° with 10 ml of 85% formic acid and 10 ml of concentrated hydrochloric acid. The mixture was diluted with water and the oil that separated was removed, dried, and shaken with 50 ml of concentrated ammonia solution (6 days at 20°). After the usual treatment, we obtained 1.7 g of (VI). Yield 45%. After recrystallization from aqueous alcohol, a white, crystalline compound was obtained that melted at 292° (with decomp.).

Tyrosine (II) from p-methoxyphenylalanine (VI). 1.7 g of (VI) was dissolved in 15 ml of acetic anhydride and 1.5 g of red phosphorus and 15 ml of hydriodic acid were added. After heating for 4 hours, cooling, and neutralization, 1.4 g of (II) was obtained. Yield 90%. After reprecipitation from alkali solution, a white, fluffy powder was obtained with m. p. 298° (with decomp.). Literature data: m. p. 298-299°; 311-313° (with decomp.) [11].

p-Chlorophenylalanine (VII). From 3 g of α-chloro-β-(p-chlorophenyl)propionic acid (XVI) and 100 ml of aqueous ammonia (7 days at 20° on a shaker) we obtained 0.77 g of (VII) with m. p. 239° (with decomp.). Yield 30%.

From 3 g of (XVI), 1 g of ammonium chloride, and 50 ml of liquid ammonia we obtained 2.15 g of (VII) with m. p. 238-239° (with decomp.). Yield 83%. Literature data: m. p. 236-241° [9], 253° [12].

p-Bromophenylalanine (IX). From 5 g of α-chloro-β-(p-bromophenyl)propionic acid, 3 g of ammonium chloride, and 100 ml of liquid ammonia (20°, 3 days) we obtained 3.94 g of (IX) as colorless plates with m. p. 254-255° (with decomp.). Yield 85%. Literature data: m. p. 258° (with decomp.) [13].

2,4-Dichlorophenylalanine (VIII). From 4.2 g of α-chloro-β-(2,4-dichlorophenyl)propionic acid, 3 g of ammonium chloride, and 100 ml of liquid ammonia we obtained 3.5 g of (VIII) with m. p. 237-239° (with decomp.) as needle-like crystals. Yield 96%. Literature data: m. p. 238-240° (with decomp.) [14].

p-Nitrophenylalanine (V). Five g of (X) was dissolved in 50 ml of dioxane and boiled with 18 g of urotropine for 4 hours. After cooling the precipitate was filtered off and washed with chloroform to remove the urotropine, then treated with an alcoholic solution of HCl, diluted with water, and boiled for 2 hours. After treatment with ammonia and evaporation, 3.28 g of (V) was obtained with m. p. 240-245° (with decomp.); the preparation darkened at 215-220°. Yield 72%. Literature data: m. p. 240-245° (with decomp.) [15].

Hydrochloride of the ethyl ester of phenylalanine from α-chloro-β-phenylpropionitrile (III). From 12 g of (III) and 30 g of urotropine in 100 ml of dioxane (boiling for 3 hours) we obtained by a method similar to that described above 4.95 g (30%) of the hydrochloride of the ethyl ester of phenylalanine with m. p. 126-127° (rosy-white plates). Literature data: m. p. 127° [16].

Hydrochloride of the ethyl ester of p-nitrophenylalanine from α-chloro-β-(p-nitrophenyl)propionitrile (IV). From 10 g of (IV) and 30 g of urotropine in 100 ml of dioxane (boiling for 3 hours) we obtained 5.2 g (40%) of the hydrochloride of the ethyl ester of p-nitrophenylalanine as lemon-yellow crystals with m. p. 177-180°. Literature data: m. p. 179-180° [13].

α-Methyl-β-phenylalanine (XI). From 15 g of α-chloro-β-phenylisobutyric acid and 35 g of urotropine in 200 ml of dioxane we obtained by the usual method (refluxing for 3 hours) 10.6 g (65%) of the hydrochloride (XI) with m. p. 236° (with decomp.). Literature data: m. p. 241-143° [8].

α-Methyl-β-(p-nitrophenyl)alanine (XVII). From 11 g of α-chloro-β-(p-nitrophenyl)isobutyric acid and 30 g of urotropine in 200 ml of dioxane (boiling for 3 hours) we obtained 8.2 g (70%) of the hydrochloride (XVII) with m. p. 273-274°. Literature data: m. p. 275-277° [8].

N,β-Diphenylalanine (XVIII) from aniline and α-chloro-β-phenylpropionitrile (III). In a flask with a reflux condenser we heated 5 g of (III) and 9.8 g of aniline on an oil bath at 130-140° for 8 hours. After cooling, the mixture was treated with 50 ml of water, and the oil was separated and subjected to hydrolysis with alcoholic potassium hydroxide (2 g of KOH per 25 ml of alcohol and 10 ml of water), the excess aniline was steam distilled off, and the contents of the flask were quickly filtered, cooled, and acidified with concentrated sulfuric acid; 2.8 g of (XVIII) was obtained as a white, crystalline powder with m. p. 172-173°. Yield 41%. Literature data: m. p. 173° [17].

SUMMARY

1. A method has been developed for the synthesis of β-aryl-α-amino acids by the amination of α-halo-β-arylpropionic and α-halo-β-arylisobutyric acids with concentrated aqueous ammonia solution, liquid ammonia, and urotropine.

2. The conversion of α-halo-β-arylpropionitriles to amino acids has been investigated.

LITERATURE CITED

[1] G. J. Martin, R. Brendel and J. M. Beiler, Exptl. Med. Surg. 8, 5 (1950).

[2] R. Gaudry, Can. J. Research, 26B, 773 (1948).

[3] L'Eckyer and A. Olivier, Can. J. Research, 28B, 648 (1950).

[4] V. I. Maimind, K. D. Ermolaev and M. M. Shemiakin, J. Gen. Chem. 26, 2313 (1956).*

[5] A. V. Dombrovskii, A. P. Terent'ev, and A. M. Iurkevich, J. Gen. Chem. 27, 419 (1957).*

[6] A. V. Dombrovskii, A. P. Terent'ev and A. M. Iurkevich, J. Gen. Chem. 26, 3214 (1956).*

[7] A. V. Dombrovskii, A. M. Iurkevich and A. P. Terent'ev, J. Gen. Chem. 27, 3346 (1957).*

[8] Stein, Brouner, J. Am. Chem. Soc. 77, 700 (1955).

[9] J. H. Burckhalter and V. C. Stephens, J. Am. Chem. Soc. 73, 56 (1951).

[10] V. V. Feofilaktov and E. V. Vinogradova, J. Gen. Chem. 13, 363 (1943).

[11] Beilst. 14, 621 (1931).

[12] A. H. Cook, G. Harris, J. R. A. Pollock and J. M. Swan, J. Chem. Soc. 1950, 1947.

[13] A. Dornow and G. Winter, Ber. 84, 307 (1951).

[14] J. H. Burckhalter and V. C. Stephens, J. Am. Chem. Soc. 73, 3502 (1951).

[15] Curtius and Mülhäuser, J. pr. Ch. 125, 298 (1930).

[16] Dictionary of Org. Compounds, I, 88 (1949).

[17] S. Kaneo, J. Pharm. Soc. Japan, 58, 256 (1938); Ch. A. 4148 (1938).

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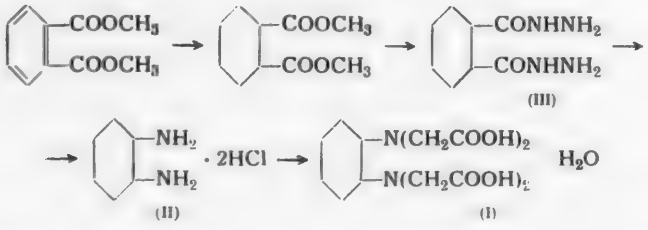
SUBSTANCES CAPABLE OF FORMING COMPLEXES

I. SYNTHESIS AND STRUCTURE OF "COMPLEXON-IV" – 1,2-DIAMINOCYCLOHEXANE-N,N,N',N'-TETRAACETIC ACID

V. G. Iashunskii and M. N. Shchukina

According to patent data [1], "Complexon-IV" – 1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid (I) – the most effective of the presently known complexons [2] – is obtained by the condensation of 1,2-diaminocyclohexane (II) with chloroacetic acid or with formaldehyde and sodium cyanide. In addition, it is pointed out [1] that the diamine is synthesized starting with anthranilic acid by the method of Einhorn [3] by reduction with metallic sodium in alcohol and subsequent conversion to the ester, amide, and (by the Hofmann reaction) diamine. Both this and other methods of preparation described in the literature for (II) [4-6] are not very suitable for producing (I) in adequate amounts.

We have developed a convenient method for preparing 1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid starting with the available dimethyl (or diethyl) phthalate; in this we have utilized data from the work of Wieland et al., [4], who synthesized (II) from the dihydrazide of cyclohexanedicarboxylic-1,2 acid (III) by the Curtius reaction. By our method (I) is obtained in four stages according to the following diagram:



Hydrogenation of dimethyl phthalate is carried out over Raney nickel under 50-100 atm. pressure and at a temperature of 110-140° without a solvent. From the hexahydro diester, by many hours' boiling with excess hydrazine hydrate, we obtain (III), which then is converted by the Curtius reaction (without isolation of the intermediate diazide and diurethane) to the dihydrochloride of 1,2-diaminocyclohexane (II). 1,2-Diaminocyclohexane-N,N,N',N'-tetraacetic acid is prepared by the reaction of the dihydrochloride of the diamine with monochloroacetic acid in the presence of alkali. The tetraacetic acid thus synthesized has all the properties of the "Complexon-IV" described in the literature.

On the basis of the high complex-forming ability of (I) Schwarzenbach [7] suggested that the nitrogen atoms in this compound have a cis-configuration with respect to the cyclohexane ring; Prishibil [2] also pointed out that the existence of trans-derivatives of (I) was unknown up to that time. However, there is no experimental evidence supporting the cis-configuration (I). For the cyclohexane ring, which can assume a "bed" form and a "chair" form, the spatial arrangement of the two neighboring substituents in the cis- and trans-isomers can differ little from one another; therefore, the a priori assumption that just the cis-configuration of "Complexon-IV" is required by its high complex-forming ability is, in our opinion, not entirely justified. For the purpose of clarifying the configuration of (I), we carried out a proof of the structure of the 1,2-

diaminocyclohexane that we prepared. Jaeger [5] showed that 1,2-diaminocyclohexane synthesized by the reduction of the dioxime of cyclohexanedione-1,2 with sodium in alcohol had the trans-structure; however, he actually did not describe derivatives of this amine. We repeated the work of Jaeger and the diamines obtained by the two methods (from the dioxime and from the dihydrazide) gave identical derivatives, corresponding in their properties to the derivatives of 1,2-diaminocyclohexane synthesized by Einhorn [3]. Consequently, the 1,2-diaminocyclohexane prepared by us and that from which (I) was prepared according to the patent data had the trans-configuration. From this it follows that "Complexon-IV" also is trans-1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid.

Comparison of the magnitudes of the apparent dissociation constants and the stability constant of the Ca-complex (CaX^{-2}) of the tetraacetic acid obtained by us (determined by the potentiometric method) with those given in the work of Schwarzenbach [7] for the corresponding values for (I) again shows conclusively that the two tetraacetic acids are identical and that "Complexon-IV" has the trans-configuration (see Table 1).

TABLE 1

	Inverse logarithms of apparent dissociation constants*				Stability constant of the complex CaX^{-2}, where X is the tetra-acid group, K_{Ca}*
	pK_1	pK_2	pK_3	pK_4	
"Complexon-IV" [7]	2.4	3.5	6.12	11.70	$10^{12.5}$
Trans-diaminocyclohexane-N,N,N',N'-tetraacetic acid	2.7**	3.6**	6.15	11.70	$10^{12.5}$

*In 0.1 M KCl solution at 20°.

**The difference in values is connected with the lesser resolving power of our potentiometer.

EXPERIMENTAL

Dimethyl ester of cyclohexane-1,2-dicarboxylic acid. By the hydrogenation of 262 g of dimethyl phthalate over 6 g of nickel catalyst in an autoclave with a volume of 2 l at 110-140° and an initial pressure of 80-100 atm (1.5-2 hours) we obtained 256 g (95%) of dimethyl ester of cyclohexane-1,2-dicarboxylic acid with b. p. 140° at 26 mm; n_D^{20} 1.4618.

Dihydrazide of cyclohexane-1,2-dicarboxylic acid (III). One-hundred g of the hexahydro diester was added over the course of 8 hours to 75 g of 100% hydrazine hydrate, which was heated to boiling in a 1-liter round-bottomed flask connected with a reflux condenser and dropping funnel. The mixture was heated at 130-135° (temperature of oil bath) for 24 hours more and the solid white mass that formed was dissolved in 1 liter of boiling water. The crystals that precipitated on cooling were separated with suction, washed with cold water and alcohol, and dried in an oven at 110°. From the mother liquor it was possible to isolate some additional quantity of the dihydrazide. In all we obtained 73-74.5 g of dihydrazide with m. p. 227-230°, which amounted to a yield of 73-74.5% calculated on the hexahydro diester. After recrystallization from water and drying, m. p. 229-231°.

Found %: C 47.86; H 8.09; N 27.75. $C_8H_{16}O_2N_4$. Calculated %: C 48.00; H 8.05; N 27.98.

Dihydrochloride of trans-1,2-diaminocyclohexane (II). Fifty g of the dihydrazide (III) was added to 170 ml of 10% hydrochloric acid in a three-necked flask, fitted with a mechanical stirrer, thermometer, and dropping funnel, while the contents were cooled (16-20°), and in the course of 20-25 minutes a solution of 34.5 g of sodium nitrite in 75 ml of water was introduced, while the temperature of the mixture was kept

TABLE 2

Titration of Tetra-Acid with 0.1 M KOH at 20°, μ = 0.1

$C_T \cdot 10^{-4}$ [a]	In the absence of Ca^{++}						In the presence of Ca^{++} ($CaCl_2$); C_{Ca} = 0.01			
	1.000	1.320	1.427	3.454	3.560	3.772	3.880	2.540	2.755	2.955
	9.97	9.95	9.94	9.76	9.75	9.73	9.72	9.80	9.78	9.76
[H]	$3.16 \cdot 10^{-4}$	$1.86 \cdot 10^{-4}$	$1.48 \cdot 10^{-4}$	$3.16 \cdot 10^{-11}$	$2.34 \cdot 10^{-11}$	$1.51 \cdot 10^{-11}$	$1.26 \cdot 10^{-11}$	$1.48 \cdot 10^{-4}$	$1.32 \cdot 10^{-4}$	$1.10 \cdot 10^{-4}$

Notes: a) number of moles of KOH consumed per mole of tetra-acid, C_T – concentration of tetra-acid. $pK_1 = 2.7$; $pK_2 = 3.6$; $pK_3 = 6.15$; $pK_4 = 11.70$; $pK'_3 \times pK_4 = 7.3$; $\log K_{Ca} = 12.5$; $K_{Ca} = 10^{12.5}$.

within the limits 18-20°. After a brief period of stirring, the aqueous solution was extracted with 400 ml of methylene chloride. 250 ml of anhydrous ethyl alcohol was added to the dried extract, and after the methylene chloride was distilled off (below 75°) the mixture was refluxed for 2 hours. After this, 350 ml of 40% sodium hydroxide solution was added and the mixture was steam-distilled in a flask with a drip trap. In 4-5 hours the distillation was completed and the distillate was acidified with hydrochloric acid. After evaporation to dryness, 26-29 g of the dihydrochloride of 1,2-diaminocyclohexane was obtained, which could be recrystallized from dilute hydrochloric acid. M. p. 232-326° (decomp.).

Found %: Cl 37.78; N 14.90. $C_6H_{14}N_2 \cdot 2HCl$. Calculated %: Cl 37.91; N 14.97.

By reduction of the dioxime of cyclohexane-1,2-dione with metallic sodium in ethyl alcohol [4] we obtained the dihydrochloride of trans-1,2-diaminocyclohexane (yield 51%) with m. p. 322-325° (from 10% HCl).

Both samples of the diamine dihydrochloride gave identical derivatives: a) diacetyl derivative with m. p. 263-264° (from a mixture of ethyl acetate and ethyl alcohol);

b) dibenzoyl derivative with m. p. 340-343° (from glacial acetic acid).

Found %: C 74.22; H 6.91. $C_{20}H_{22}O_2N_2$. Calculated %: C 74.50; H 6.88.

c) dibenzene sulfonyl derivative with m. p. 153-155° (from 40% ethyl alcohol).

Trans-1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid. Seventy-eight ml of 25% solution of sodium hydroxide (chem. pure) was added, with external cooling, to 59 g of monochloroacetic acid, and then 23.35 g of diamine dihydrochloride (II) was introduced. While the mixture was stirred and heated on a boiling water bath, 25% sodium hydroxide solution was added at such a rate that a sample continuously colored thymolphthalein paper blue. In 10-15 minutes about 80 ml of the alkali was used, i.e., the principal amount. Heating and stirring of the mixture was continued for 3 hours more, during which time another 15-20 ml of alkali was added. The hot solution was acidified with concentrated hydrochloric acid (17-20 ml) and treated with activated carbon, and by further addition of concentrated hydrochloric acid (about 25 ml to a pH of 1.5-2) the tetraacetic acid was precipitated; this was then washed with distilled water and dried at 60-70°. 24.4 g of the monohydrate of trans-1,2-diaminocyclohexanetetraacetic acid was obtained (53.5% calculated on the dihydrochloride, which could be recrystallized from a large amount of water for complete purification.

Found %: C 46.20; H 6.56; H_2O 4.86. $C_{14}H_{22}O_8N_2 \cdot H_2O$. Calculated %: C 46.15; H 6.64; H_2O 4.94.

Upon heating to 100° under reduced pressure the monohydrate split out a molecule of water.

Potentiometric determination and calculation of the dissociation constant were carried out by the method of Schwarzenbach [8], employing the data of Martell and Calvin [9]. A LP-5 potentiometer was used for the work. By way of example, the results of one of the parallel titrations are presented (see Table 2).

SUMMARY

1. A convenient method has been developed for the preparation of trans-1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid.

2. It has been shown that the "Complexon-IV" described in the literature has the trans-configuration.

LITERATURE CITED

[1] Swiss Patent 264,883 (1950); Chem. Abs. 45, 2020 (1951); U. S. Patent 2,519,708; Chem. Abs. 45, 6218 (1951).

[2] R. Prishibil, Complexons in Chemical Analysis. M. (1955).*

[3] A. Einhorn and B. S. Bull, Lieb. Ann. 295, 209 (1897).

[4] H. Wieland, O. Schlichting and W. Langsdorf, Z. physiol. Ch. 161, 76 (1926).

[5] F. M. Jaeger and L. Bijkerk, Kon. Akad. Wetensch. Amsterdam Proc. 40, 12 (1937); Zbl. 1937, II, 1196.

[6] H. Baldock, N. Levy and C. W. Scaife, J. Chem. Soc. 1949, 2627.

[7] G. Schwarzenbach and H. Ackermann, Helv. Chim. Acta. 32, 1682 (1949).

[8] G. Schwarzenbach et al., Helv. Chim. Acta. 30, 1303, 1798 (1947).

[9] A. E. Martell and M. Calvin, Chemistry of the Metal Chelate Compounds, N. Y., 92 (1952).

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*In Russian.

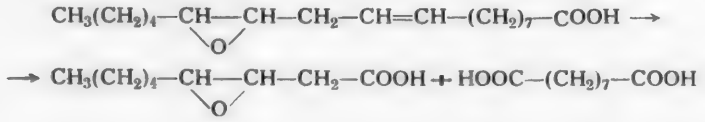
METHYL LINOLEATE MONOXIDE AND ITS PROPERTIES

G. V. Pigulevskii and I. N. Naidenova

In 1929 a report was published by one of us with A. Ia. Vasil'ev [1, 2] on the preparation of a dioxide of methyl linoleate (m. p. 32.1°) and a liquid isomer of it. On saponification of the crystalline isomer a dioxide of linoleic acid (m. p. 76.4°) was isolated. In the same year articles by Böeseken et al., appeared [3, 4], in which the authors obtained the same results. The question of the possibility of obtaining an unsaturated monoxide of linoleic acid remained open. It was found, however, that the oxidation of methyl linoleate by benzoyl hydrogen peroxide goes stepwise: first one double bond is oxidized, the second double bond being oxidized considerably more slowly. It is also known that hydrogenation [5] and bromination [6] of linoleic acid proceed in two phases. The multiple bonds of linoleic acid, consequently, have a different reactivity. All this provided a basis for us to assume that the synthesis of a monoxide of linoleic acid could be accomplished.

To carry this out, the methyl ester of linoleic acid was oxidized with acetyl hydrogen peroxide prepared (to avoid contamination with acetyl peroxide) from boroacetic anhydride. The monoxide of methyl linoleate was a colorless oil with b. p. 173-175° (0.08 mm).

The structure of the monoxide was demonstrated on the basis of its oxidation by potassium permanganate in acetone solution. If the oxygen ring was on the 12 and 13 carbon atoms, we should find the oxide of nonenoic acid and azelaic acid among the oxidation products.



But if the oxygen ring was formed with the 9 and 10 carbon atoms, then the oxidation products should be caproic acid $C_6H_{12}O_2$, and the oxide of dodecenoic acid.

As a result of the oxidative decomposition of the monoxide of linoleic acid we isolated azelaic acid and the oxide of nonenoic acid (m. p. 56-57°), from which we obtained the barium salt. In addition, acetic and, apparently, caproic acids were found among the oxidation products that were volatile with steam. The two latter acids could be produced only as a result of breakdown of the oxide of nonenoic acid, since the oxide of dodecenoic acid was not found in the oxidation products.

However, we did not wish to be limited by these data. To clarify the structure of the monoxide of linoleic acid it was necessary to obtain the hydrogenated monoxide of this acid. If the hydrogenated oxide had the structure of the oxide of 6-octadecene-18-carboxylic acid, its properties should be different from those of the oxide of oleic acid (i.e., the oxide of 9-octadecene-18-carboxylic acid).

Actually an oily liquid with b. p. 190.5-191.0° (0.7 mm) was obtained by the hydrogenation of the monoxide of methyl linoleate. By saponification of this product an oxide was produced (m. p. 18.5-19.6°) that differed in its properties from the oxide of oleic acid. On reaction with ammonia [7] it gave a hydroxyaminostearic acid with m. p. 84-85°.•

• The hydroxyaminostearic acid prepared from the oxide of oleic acid melted at 154-155°.

The monoxide of methyl linoleate had unusual properties that were dependent on the proximity of the oxygen ring to the double bond. In our first experiments on catalytic hydrogenation of the unsaturated monoxide obtained by us, a high reactivity was observed for the double bond. Having encountered this phenomenon, we carried out a comparative hydrogenation of methyl linoleate and the methyl ester of the oxide of linoleic acid. As can be seen from the figure, addition of the hydrogen necessary to saturate one double bond proceeded at the same rate for both compounds. Thus, the results of hydrogenation showed that the double bond in the linoleic acid monoxide molecule has the same activity, as the most reactive double bond (Δ^{12}) of linoleic acid.

EXPERIMENTAL

Preparation of methyl linoleate. The starting material for the synthesis of linoleic acid was linoleic acid tetrabromide obtained directly from the mixed acids of sunflower oil. The tetrabromide was characterized by its m. p. 114.5°. Yield 47%. The linoleic acid was synthesized from the tetrabromide by treatment of the latter with zinc in pyridine solution by the method of Kaufmann.

It was found experimentally that the best weight ratio of zinc, tetrabromide, and pyridine was 1:1:2. The zinc was used in the form of thin flakes, purified of zinc oxide.

The linoleic acid synthesized in this way was esterified in the presence of methyl alcohol saturated with hydrogen chloride. The methyl linoleate boiled at 196-197° (8 mm). The yield based on the bromide employed was 45.2%.

Found: iodine number 172.05, 171.50. $C_{19}H_{34}O_2$. Calculated: iodine number 172.79.

Synthesis of the monoxide of methyl linoleate. Acetyl hydrogen peroxide was made from boroacetic anhydride. To a solution of 58 g of methyl linoleate in 300 ml of ether was added 200 ml of an ethereal solution of acetyl hydrogen peroxide (containing 3.31 g of active oxygen). Spontaneous heating of the reaction mixture was not observed. The reaction was completed in 45 hours. On fractional distillation of the oxidized methyl linoleate a fraction was isolated with b. p. 195-197° (6 mm).

d_4^{20} 0.9376, n_D^{20} 1.4600. MR_D 90.56. calc. 90.57.

Found %: C 72.78, 72.93; H 11.21, 11.06; iodine number 81.1, 81.6; ester number 181.10, 183.14. $C_{19}H_{34}O_3$. Calculated %: C 73.48; H 11.06; iodine number 81.93; ester number 180.97.

Monoxide of linoleic acid. The monoxide of methyl linoleate was saponified and the free monoxide of linoleic acid was separated from the saponification products by the usual methods as a yellowish oil that solidified on cooling to fine crystals (m. p. 18-19°). Soluble in methyl alcohol and in ethyl and petroleum ethers.

Oxidation of the monoxide of linoleic acid with potassium permanganate.

To 150 ml of acetone was added 1.8 g of $NaHCO_3$. 8.7 g of linoleic acid monoxide was added to the suspension that was obtained, and then powdered potassium permanganate was added in small portions, with cooling with ice water and continuous shaking, until decoloration ceased. In all 40.5 g of $KMnO_4$ was added. Then the acetone was removed from the reaction mixture by distillation. The residue was washed 5 times with 5% KOH solution. The combined wash waters were concentrated to 200 ml and acidified with sulfuric acid. The acid solution was extracted with ethyl ether. The residue obtained after removal of the ether from the solution was treated with steam. In the distillation flask, upon cooling, a white precipitate separated out, which was dissolved in an excess of hot water. A layer of oil that came to the surface on cooling was extracted with ether. From the aqueous solution that had been concentrated to 50 ml a crystalline precipitate separated on cooling with ice. After recrystallization from water it melted at 105.8°. A mixed sample with azelaic acid did not give a depression in melting point.

Found: neutralization equivalent 303.96, 304.70. $C_9H_{16}O_4$. Calculated: neutralization equivalent 304.58.

The ether was removed from the ethereal solution that was obtained by treatment of the contents of the distillation flask. The residue, which consisted of an oil and crystals, was washed with water to remove traces of azelaic acid. The dried product melted at 56-57°.

Found: neutralization equivalent 341.0, 324.6. $C_9H_{16}O_3$. Calculated: neutralization equivalent 326.0.

After neutralization with ammonia and addition of $BaCl_2$, the barium salt of the oxide of nonenoic acid precipitated.

Found %: Ba 28.31, 28.9. $(C_9H_{15}O_3)_2Ba$. Calculated %: Ba 28.64.

From the distillate obtained on treatment of the oxidation product with steam a mixture of two acids was extracted, one of which seemed readily soluble in water, and the other in alcohol. Barium salts were obtained from both acids.

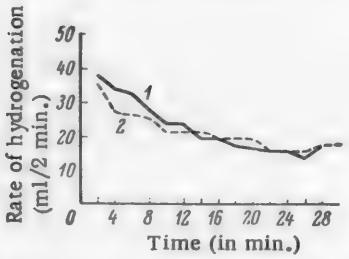
Ba salt of acid soluble in water.

Found %: Ba 52.52. $(C_2H_3O_2)_2Ba$. Calculated %: Ba 53.2.

Ba salt of acid soluble in alcohol.

Found %: Ba 35.24. $(C_8H_{11}O_2)_2Ba$. Calculated %: Ba 37.2.

Catalytic hydrogenation of the monoxide of methyl linoleate. 2.2359 g of the monoxide, 10 ml of ethyl alcohol, and 0.103 g of catalyst (PtO_2) were shaken in an atmosphere of hydrogen. The total volume of hydrogen absorbed was 311 ml at 18° and 774 mm (calculated 306 ml). The volume of hydrogen absorbed for each 2 minutes (rate of hydrogenation) was: 34, 27, 25, 26, 21, 21, 21, 19, 19, 20, 15, 17, 13, 16, 17 ml (see Figure).



Graph of comparative catalytic hydrogenation of methyl linoleate and methyl ester of linoleic acid monoxide. 1) Methyl linoleate, 2) methyl ester of linoleic acid monoxide.

The hydrogenation product, after removal of the alcohol and traces of methyl stearate (m. p. 37°) that were formed, was distilled twice in vacuo. By distillation a fraction was obtained with b. p. 190.5-191° (7 mm) that was a clear liquid with a slight odor.

d_4^{20} 0.9319, n_D^{20} 1.45307, MR_D 90.58; calc. 91.03.

Found %: C 72.62, 72.45; H 11.45, 11.68; ester number 180.38, 180.44. $C_{19}H_{36}O_3$. Calculated %: C 73.03; H 11.61; ester number 179.5.

Addition of ammonia to the oxide of 6-octadecene-18-carboxylic acid. 0.98 g of the oxide and 10 ml of concentrated ammonia solution were placed in a thick-walled ampoule. The sealed ampoule was heated in a thermostat at 120° for 10 hours. Then the contents of the ampoule, a clear liquid, were poured into a porcelain dish and allowed to stand for two days. As the ammonia evaporated, a white cloud began to appear. The remaining ammonia was removed in a vacuum desiccator. A slightly yellowish mass readily soluble in alcohol, remained in the dish. From the alcohol solution crystals of hydroxyaminostearic acid with m. p. 84-85° precipitated on cooling.

SUMMARY

The monoxide of methyl linoleate had the structure of the methyl ester of 12,13-oxido-9-octadecene-1-carboxylic acid. By hydrogenation of this compound the oxide of the methyl ester of 6-octadecene-18-carboxylic acid was formed.

It has been made clear that the double bond of the methyl ester of 12,13-oxido-9-octadecene-1-carboxylic acid is hydrogenated at the same rate as the double bond of Δ^{12}-methyl linoleate.

LITERATURE CITED

[1] G. V. Pigulevskii, J. Russ. Chem. Soc. 48, 1763 (1916).

[2] G. V. Pigulevskii and A. Ia. Vasil'ev, J. Russ. Chem. Soc. 61, 988 (1929); J. Gen. Chem. 1, 235 (1931).

[3] J. Böeseken, W. C. Smit and A. H. Gaster, Proceeding Ac. Sci. Amsterdam 32, 377 (1929).

[4] W. Smit, Rec. trav. chim. 49, 615 (1930).

[5] Y. Inoe and B. Suzuki, Proc. Imp. Acad. Tokyo 7, 15 (1931).

[6] J. Toyama and T. Tutiya, J. Chem. Ind. Japan, 38, 35 (1931).

[7] G. V. Pigulevskii and I. L. Kuranova, Proc. Acad. Sci. USSR, 82, 601 (1952).

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INVESTIGATION OF AROMATIC COMPOUNDS WITH A LONG SIDE CHAIN

II. PREPARATION OF DODECYLANILINE BY AMMONOLYSIS OF p-CHLORODODECYLBENZENE

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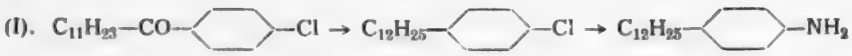
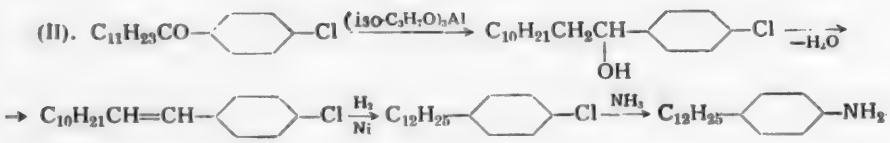
It is known that homologs of aniline can be prepared by the reduction of the corresponding nitro compounds [1]; however, there are no data in the literature on the preparation of p-n-dodecylaniline by this method. There are directions in the literature for the preparation of p-dodecylaniline in small yields by the catalytic isomerization of N-dodecylaniline at temperatures below 240° in the presence of $ZnCl_2$ and $CoCl_2$ [2, 3]. The isomerization is accompanied by a large amount of by-products.

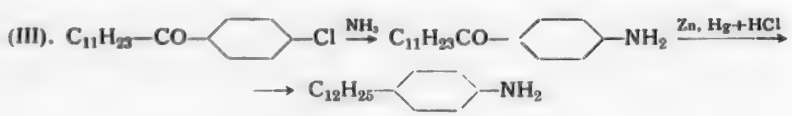
In our previous communication [4] it was shown that p-n-dodecylaniline, like a number of other homologs of aniline containing a normal aliphatic chain in the para position to the amino group, can be obtained by the reduction of alkyl (4-aminophenyl) ketones with amalgamated zinc and hydrochloric acid. In the present work we describe the preparation of p-n-dodecylaniline by the replacement of chlorine by the amino group in p-chlorododecylbenzene, which in turn was prepared from p-chlorolaurophenone by two different methods, namely by the reduction in one stage of p-chlorolaurophenone by a modified Kishner method [5] and by a poly-stage method: first p-chlorolaurophenone was reduced with aluminum isopropylate to dodecyl-(4-chlorophenyl)carbinol, the carbinol was further dehydrated in vacuo over potassium bisulfate heated to 200°, and finally the p-chlorododecenylbenzene obtained was hydrogenated on a Raney nickel catalyst.



In spite of the many-stage procedure, the yield of p-chlorododecylbenzene by the second method was higher (75%) than by the reduction of p-chlorolaurophenone by the Kishner method (65.7%). The p-chlorododecylbenzene was further converted to p-dodecylaniline by heating it for 6 hours with 30% aqueous ammonia solution to 250° in the presence of cuprous chloride.



In comparing the methods for the preparation of dodecylaniline, it should be pointed out that the yield based on the starting p-laurophenone by Scheme I was 54.5%, and that by Scheme II was 60%, while it did not exceed 47.5% when the compound was prepared through undecyl (4-aminophenyl) ketone (Scheme III).



By direct alkylation of aniline with alcohols in the presence of $ZnCl_2$ [3], p-dodecylaniline was obtained as the main reaction product with a yield up to 32%.

EXPERIMENTAL

Preparation of undecyl-(4-chlorophenyl)carbinol [6]. 29.5 g of p-chlorolaurophenone and 100 ml of 1 M aluminum isopropylate solution were heated on a water bath in a flask with a Gan* dephlegmator until there was a negative reaction in the distillate for acetone (test with 2,4-dinitrophenylhydrazine). After most of the isopropyl alcohol was distilled off in vacuo and the reaction mixture was cooled, the residue was treated with dilute hydrochloric acid (1:2) and the undecyl-(4-chlorophenyl)carbinol was extracted with benzene. After the solvent was distilled off from the solution, which had been dried with sodium sulfate, the product was distilled in vacuo. 27.9 g (94%) of undecyl-(4-chlorophenyl)carbinol was obtained with b. p. 207.5° (at 5 mm), freezing point 22.5°, n_D^{25} 1.5042.

Found %: C 72.96, 72.83; H 9.99, 9.86; OH 5.70, 5.67. $C_{18}H_{29}OCl$. Calculated %: C 72.83; H 9.85; OH 5.73.

Preparation of p-chlorododecenylbenzene. To 8.2 g of fused, finely pulverized potassium bisulfate, heated to 200° at a residual pressure of 10 mm, was added dropwise 16.5 g of undecyl-(4-chlorophenyl)carbinol. When addition of the carbinol was finished, the mixture was heated at the indicated temperature for another 20 minutes and the product was then distilled at a bath temperature of 230°. 13.5 g (86.5%) of p-chlorododecenylbenzene was obtained. On repeated distillation a product was obtained with b. p. 214° (at 10 mm), freezing point 25°, $n_D^{25.5}$ 1.5200.

Found %: C 77.83, 77.68; H 9.86, 9.95. $C_{18}H_{27}Cl$. Calculated %: C 77.54; H 9.76.

Preparation of p-chlorododecylbenzene by reduction of p-chlorododecenylbenzene. 27.9 g of p-chlorododecenylbenzene in 70 ml of anhydrous alcohol was reduced at atmospheric pressure on 1.5 g of Raney Ni. 2240 ml of hydrogen was absorbed in 7 hours. After removal of the nickel, the catalyzate was diluted with an equal amount of water, and the oily layer was separated, dried with calcium chloride, and distilled. 25.5 g (91.2%) of p-chlorododecylbenzene was obtained with b. p. 196.5° (at 5 mm), freezing point 9.5°, n_D^{20} 1.4920, d_4^{20} 0.9361.

Found %: C 77.33, 77.20; H 10.51, 10.39. $C_{18}H_{29}Cl$. Calculated %: C 76.96; H 10.41.

Reduction of p-chlorolaurophenone by a modification of the Kishner method. A mixture of 12 g of p-chlorolaurophenone, 52 ml of diethylene glycol, 5.2 g of sodium hydroxide, and 20 ml of hydrazine hydrate was heated on a boiling water bath with vigorous stirring for 24 hours. Then the temperature was slowly raised to 185° and the hydrazine hydrate partially distilled off. The mixture was kept at this temperature for 8 hours. On completion of the reduction, the mass was poured into water and the p-chlorododecylbenzene was extracted with ether. After the ether was distilled off, the product was distilled in vacuo. 7.5 g (65.7%) of p-chlorododecylbenzene was obtained with b. p. 213.5° (at 15-17 mm), freezing point 9.5°, n_D^{20} 1.4925.

Found %: C 77.10, 76.88; H 10.53, 10.49. $C_{18}H_{29}Cl$. Calculated %: C 76.96; H 10.41.

Preparation of p-dodecylaniline. 10.7 g of p-chlorododecylbenzene, 1.2 g of copper chloride, and 300 ml of 30% ammonia solution were heated at 250° in an autoclave for 6 hours. After extraction from the reaction mass with ether, the dodecylaniline was isolated as the hydrochloride by passing a current of dry hydrogen chloride through the ethereal solution. 8.6 g (80.2%) of dodecylaniline hydrochloride was obtained. To isolate the free amine, the hydrochloride was treated with 10% sodium hydroxide solution. A product was obtained with m. p. 40.5-41°. A mixed sample with dodecylaniline prepared by the reduction of p-aminolaurophenone (m. p. 41.5-42°) gave no depression in melting point.

SUMMARY

1. p-Chlorolaurophenone has been reduced to dodecyl-(4-chlorophenyl)-carbinol, by the dehydration

* Transliteration of Russian—Publisher's note.

of which p-chlorododecenylbenzene was obtained; by hydrogenation of the latter on Raney Ni p-chlorododecylbenzene was obtained.

p-Chlorododecylbenzene also was obtained by direct reduction of p-chlorolaurophenone by a modified Kishner method.

2. It has been shown that p-n-dodecylaniline can be prepared in up to 80% yield by the amination of p-chlorododecylbenzene.

LITERATURE CITED

[1] F. F. Beilstein and A. P. Kulberg, Lieb. Ann. 156, 208 (1870); E. Cline and E. Reid, J. Am. Chem; Soc. 49, 3152 (1927); R. Read and D. Mullin, J. Am. Chem. Soc. 50, 1764 (1928).

[2] A. Beran, Ber. 18, 132 (1885); French Pat. 815562; British Pat. 468226; Zbl. 1937, II, 2752; W. J. Hickinbottom, J. Chem. Soc. 1937, 1123.

[3] Azano et al., J. Chem. Soc. Japan (Industrial Chemistry Section), 59, 578 (1956).

[4] L. N. Nikolenko and K. K. Babievskii, J. Gen. Chem. 25, 2231 (1955).*

[5] Reactions and Methods of Investigation of Organic Compounds, Coll. 1, Goskhimizdat, 36 (1951).**

[6] Organic Reactions, II, 223 (1950).**

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**In Russian.

β-ACYLOXYACROLEINS

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Up until the present time β-acyloxyacroleins have remained unknown compounds of the general formula AcOCH=CH−CH=O (I) containing the reactive system of an α,β-unsaturated aldehyde and offering interest as starting materials for a number of syntheses.

We have prepared these compounds by the reaction of the sodium salt of malonic dialdehyde (II) with acid chlorides. When acetyl, propionyl, n-butyryl, or benzoyl chloride was used, satisfactory results were obtained by "method A"— treatment of the acid chloride with a suspension of the sodium salt of malonic dialdehyde in an inert solvent (see experimental section). The starting salt (II) was prepared by us by hydrolyzing 1,1,3,3-tetraethoxypropane [1] in the presence of traces of hydrochloric acid and subsequently neutralizing with sodium hydroxide solution. The reactions with p-nitrobenzoyl chloride or chlorocarbonic ester were carried considerably more conveniently by "method B," by the action of the acid halide on an aqueous solution of salt (II).

β-Acyloxyacroleins that contain an aliphatic acid group are liquids which have an acrid, characteristic odor, are distillable in vacuo, and show an exaltation of the molecular refraction; the compounds with an aromatic acyl group are crystalline substances. All the β-acyloxyacroleins are soluble in the usual organic solvents except petroleum ether; they are insoluble in water and in aqueous solutions of sodium carbonate, but are rapidly hydrolyzed by them with the formation of malonic dialdehyde. The compounds (I) do not give an immediate color reaction with ferric chloride solution; the coloration that appears later is the result of hydrolysis. They give typical reactions for the aldehyde group; in the presence of an excess of semicarbazide they form only monosemicarbazones (which are converted by heating with sodium acetate solution to the amide of pyrazole-1-carboxylic acid). They are easily condensed with salts of guanidine, forming 2-aminopyrimidine.

All of the properties that have been enumerated confirm the structures (I) for the compounds that have been prepared, and are not in keeping with the structure of the acylmalonic dialdehydes $AcCH(CH=O)_2$, the formation of which might be be expected if the acylation reaction proceeded with a shift in the reaction center.

The properties and analytical data for the β-acyloxyacroleins (I) that were prepared and for their semicarbazones are given in Tables 1 and 2.

EXPERIMENTAL

Preparation of the sodium salt of malonic dialdehyde (II). A mixture of 22 g of 1,1,3,3-tetraethoxypropane, 8 ml of 1 N HCl solution, and 20 ml of water was stirred at 50-55° until it was homogeneous. After 10 minutes' standing at room temperature, the solution was titrated slowly with 5 N NaOH solution until it was alkaline to phenolphthalein. The solution obtained was evaporated in vacuo almost to dryness (bath temperature 40-50°), and the residue was treated with a mixture of anhydrous alcohol and acetone (1:3). 8.6 g of the dihydrate of the sodium salt of malonic dialdehyde was obtained; from the mother liquor another 0.7 g of less pure material was obtained after dilution with acetone. Total yield 71%. The compound was dried to constant weight in vacuo at 60°. For analysis, the salt was dissolved in water, precipitated with acetone, and dried in vacuo.

TABLE 1

β-Acyloxyacroleins of the General Formula AcOCH=CH−CH=O

Ac	Method	Yield (% calc. on acyl halide)	B. p. or m. p.	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	Analysis (%) found •••• C	Analysis (%) found •••• H	Analysis (%) calculated C	Analysis (%) calculated H
CH_3CO	A	59	57.5—59° (at 4 mm)	1.1204	1.4703	28.27	26.49	52.37	5.52	52.68	5.25
C_2H_5CO	A	53	49—50 (at 1.5 mm)	1.0 07	1.4710	33.10	31.10	56.04	6.37	56.25	6.25
n-C_3H_7CO	A	42	67—68 (at 2.5 mm)	1.0451	1.4676	37.77	35.72	59.04	7.15	59.15	7.04
C_6H_5CO	A	80	63*	—	—	—	—	68.10	4.66	68.18	4.57
	B	47									
p-$O_2NC_6H_4CO$	B	54**	130—131***	—	—	—	—	54.52	3.30	54.30	3.17
CH_3OCO	B	55	50—50.5*	—	—	—	—	46.34	4.66	46.15	4.61

* From a mixture of ether and petroleum ether.

** Found %: N 6.23, 6.06. Calculated %: N 6.33.

*** From dioxane.

**** Average values from two determinations are given.

Found %: Na 23.89, 24.33. $C_3H_3O_2Na$. Calculated %: Na 24.45.

Preparation of β-acetoxyacrolein (method A). 1.6 g of acetyl chloride was added gradually, with stirring, to a suspension of 2.8 g of anhydrous sodium salt of malonic dialdehyde in 20 ml of anhydrous ether; the mixture was stirred at room temperature for 10 minutes more and filtered; hydroquinone was added to the filtrate, the ether was evaporated in vacuo, and the residue was distilled. 1.35 g (59% calculated on acetyl chloride) of β-acetoxyacrolein was obtained with b. p. 57.5-59° at 4 mm (Table 1).

Preparation of β-acetoxyacrolein semicarbazone. To a solution of 0.4 g of β-acetoxyacrolein in 2 ml of alcohol was added an aqueous solution of 0.4 g of semicarbazide hydrochloride and 0.54 g of sodium acetate. 0.41 g of semicarbazone was obtained with m. p. 172-173° (with decomp., from aqueous alcohol) (Table 2). A similar experiment was carried out using a triple excess of semicarbazide hydrochloride (1.2 g). As a result 0.5 g of monosemicarbazone was obtained with m. p. 172-173° (with decomp., from aqueous alcohol).

Preparation of β-(p-nitrobenzoxy)-acrolein (method B). 6.6 g of 1,1,3,3-tetraethoxypropane was hydrolyzed (method A). To the aqueous solution of salt (II) obtained after neutralization was added 30 ml of chloroform, after which a solution of 4.32 g of p-nitrobenzoyl chloride in 40 ml of chloroform was added dropwise, very slowly. The chloroform layer was washed with a sodium bicarbonate solution, then with water, and dried. The residue after evaporation of the chloroform was recrystallized from ethyl acetate. Yield of β-(p-nitrobenzoxy)acrolein 2.7 g (53% calculated on acid chloride), m. p. 129-130°. After recrystallization from dioxane, m. p. 130-131°.

Amide of pyrazole-1-carboxylic acid. A mixture of 0.4 g of β-butyroxyacrolein semicarbazone, 16 ml of 50% alcohol, and 0.26 g of crystalline sodium acetate was heated for a half hour on a boiling water bath. After the solution had cooled 0.02 g (36%) of the amide of pyrazole-1-carboxylic

TABLE 2

Semicarbazones of β-Acyloxyacroleins of the General Formula $AcOCH=CH-CH=N-NHCONH_2$

Ac	Melting point	Analysis (%)					
		found *			calculated		
		C	H	N	C	H	N
CH_3CO	172—173° (with decomp., from aq. alc.)	42.39	5.29	24.59	42.10	5.26	24.56
C_2H_5CO	154—155 (with decomp., from aq. alc.)	45.53	5.94	22.40	45.40	5.94	22.69
n.-C_3H_7CO . . .	150—151 (with decomp., from aq. alc.)	48.31	6.66	21.55	48.24	6.53	21.10
C_6H_5CO	171 (with decomp. from methanol)	56.63	4.79	18.17	56.65	4.72	18.01
p-$O_2NC_6H_4CO$ . .	173—174 (with decomp., from dioxane)	47.63	3.79	19.80	47.48	3.59	20.14
CH_3OCO	169—170 (with decomp., from aq. alc.)	38.81	4.85	22.40	38.50	4.81	22.46

acid was obtained, which did not give any depression in melting point when mixed with a sample obtained by another method [2].

2-Aminopyrimidine. 0.8 g of β-butyroxyacrolein was added dropwise, with shaking, to a solution of 0.56 g of guanidine hydrochloride in 3 ml of 18% hydrochloric acid solution. After 3 hours an excess of 40% sodium hydroxide solution was added, the thick mass was dried in a desiccator and extracted with hot benzene. 0.27 g (51%) of 2-aminopyrimidine was obtained with m. p. 124-125°, which did not show any depression in melting point when mixed with a sample prepared by another method [2].

SUMMARY

By the reaction of the sodium salt of malonic dialdehyde with acyl halides, a number of β-acyloxyacroleins were prepared which had the general formula

$$AcOCH=CH-CH=O,$$

where Ac is an organic acid group. The properties of this new type of compound were studied.

LITERATURE CITED

[1] T. V. Protopopova and A. P. Skoldinov, J. Gen. Chem. 27, 57 (1957).*

[2] T. V. Protopopova and A. P. Skoldinov, J. Gen. Chem. 27, 1276 (1957).*

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AUTO-OXIDATION OF A METHYLENE GROUP BOUND TO AN AROMATIC NUCLEUS

II. AUTO-OXIDATION OF THE METHYL ESTER OF 9-PHENYLUNDECANOIC ACID

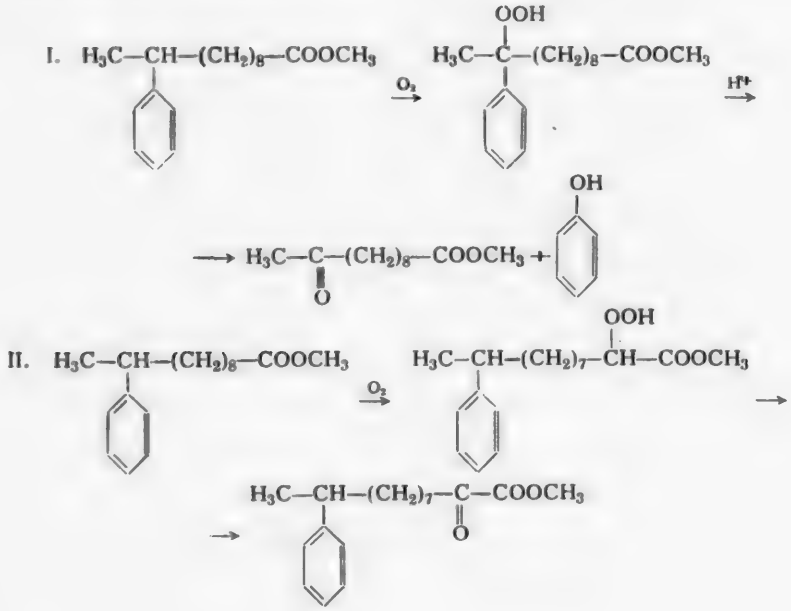
P. G. Sergeev* and A. M. Sladkov

It has been shown by us earlier [1] that the auto-oxidation of compounds, in which the methylene group being subjected to the action of oxygen is simultaneously activated by a phenyl and a carbomethoxy group, proceeds at a fairly rapid rate and in the case of the simpler compounds of this type—the esters of phenylacetic acid—leads to obtaining the esters of phenylglyoxylic acid in high yields.

We became interested in the possibility of auto-oxidizing those types of compounds in which both a phenyl group and an ester group would be present at the same time, but at a sufficient distance from each other to avoid mutual influence on the group being oxidized. We prepared the methyl ester of 9-phenylundecanoic acid as being a suitable compound for studying the indicated reaction. This compound has in its molecule two active centers: the CH group, found in the α-position to the phenyl nucleus, and the CH_2 group, found in the α-position to the carbomethoxy group. The distance of nine carbon atoms between these two activating groups is apparently sufficient to exclude their mutual effect.

The primary products formed during the reaction, namely hydroperoxides, were converted into simpler products, which made their isolation and identification easier.

The possible directions of the auto-oxidation reaction and the transformations of the first formed hydroperoxides are shown below by the schemes.



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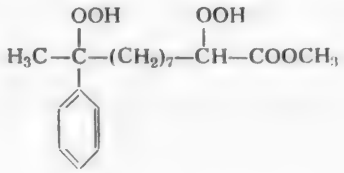
In addition to these two variations for the auto-oxidation reaction and the approximately equal activating influence of the phenyl and carbomethoxy groups, it would also be possible to obtain as a primary reaction product the bis-hydroperoxide with the structure



This hydroperoxide would also be converted into the final product: the methyl ester of 1,9-dioxoundecanoic acid.

Investigation revealed that the auto-oxidation proceeds according to Scheme I, and here a tertiary hydroperoxide is obtained, decomposing under the influence of acids into phenol and the methyl ester of 9-oxoundecanoic acid. Other oxidation products or products of their transformation were not found. This suggests that the activating influence of the phenyl group is much greater than the activating influence exerted by the ester group.

EXPERIMENTAL

Preparation of methyl ester of 9-phenylundecanoic acid. To a suspension of 43 g of anhydrous aluminum chloride in 180 ml of benzene was added 50 g of methyl undecenoate with vigorous stirring. The temperature during reaction was not permitted to rise above 25°. After all of the ester had been added the mixture was stirred for 1.5 hours (total reaction time was 3 hours). The reaction products were poured into water; the oil was separated, washed with water, 5% aqueous potash solution, again with water, and dried over anhydrous sodium sulfate.

We obtained 48.5 g (67%) of methyl 9-phenylundecanoate with b. p. 196-198° at 6 mm.

Found: ester number 135.2 mg/g. $C_{18}H_{28}O_2$. Calculated: ester number 132.7 mg/g.

Auto-oxidation of methyl 9-phenylundecanoate. The process was run in a glass column having a diameter of 12 mm, filled to 2/3 of its height with a packing of cut glass tubes 5 × 2 mm in size. Air was passed at a rate of 0.5 liter/min through 45 g of the methyl 9-phenylundecanoate at 100°. About 0.01 g of the sodium salt of cumene hydroperoxide was added to initiate the process. After 35 hours the reaction mass contained 11.2% of the hydroperoxide (calculated as the monohydroperoxide; iodometric determination). After 36 hours the hydroperoxide content dropped to 10.8%, for which reason the oxidation was terminated.

Treatment of the reaction mass. An attempt to isolate the formed hydroperoxide from the reaction mass as the sodium salt proved unsuccessful; consequently we decided to decompose the hydroperoxide without isolating it from the reaction mass. For this the oxidation products were diluted with an equal amount of benzene, and then with cooling to 5° and vigorous stirring a drop of concentrated sulfuric acid was added. The reaction mass was stirred and allowed to gradually warm up to room temperature, after which it was heated at 50-60° until a test sample gave a negative test for hydroperoxide. After this the mixture was made exactly neutral by the addition of sodium bicarbonate. Then the benzene was distilled at reduced pressure from the reaction products, and the residue was vacuum-fractionated. The following fractions were isolated: 1st fraction, b. p. 62-64° at 5 mm, 1.8 g; 2nd fraction, b. p. 144-148° at 5 mm, 1.9 g; 3rd fraction, b. p. 194-197° at 5 mm, 40.8 g.

The 1st fraction crystallized completely in the receiver and had m. p. 42°. Its mixture with a specimen of pure phenol did not depress the melting point.

The 2nd fraction was hydrolyzed with a 10% aqueous alcohol solution of sodium hydroxide. Acidification of the hydrolysis products gave an oil, which gradually crystallized. After recrystallization from petroleum ether, m. p. 58-58.5°; literature [2]: 9-oxoundecanoic acid, m. p. 59.5°.

The oxime with m. p. 69-70° (from alcohol) was obtained from the acid; literature [3]: m. p. 68-69°.

Found %: N 5.89. $C_{12}H_{23}O_3N$. Calculated %: N 6.10.

The 3rd fraction was unoxidized methyl 9-phenylundecanoate. It gave a negative test for the carbonyl group.

SUMMARY

1. Based on the auto-oxidation of the methyl ester of 9-phenylundecanoic acid it was shown that the phenyl group exerts a much greater activating influence on a carbon atom found alpha to it, than does the carbomethoxy group on a carbon atom adjacent to it.

2. The scheme for the auto-oxidation of the methyl ester of 9-phenylundecanoic acid was shown, and the decomposition products of the initially formed hydroperoxide were isolated.

LITERATURE CITED

[1] P. G. Sergeev and A. M. Sladkov, J. Gen. Chem. 27, 819 (1957).*

[2] Myddleton and Barret, J. Am. Chem. Soc. 49, 2258 (1927).

[3] Chuit, Boelsing, Hausser and Malet, Helv. Chim. Acta, 9, 1084 (1926).

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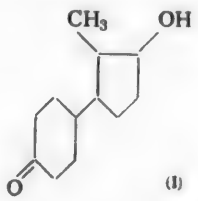
ANALOGS OF STEROID HORMONES

I. PREPARATION OF 3-(4-OXOCYCLOHEXYL)-2-METHYLCYCLOPENTANOL

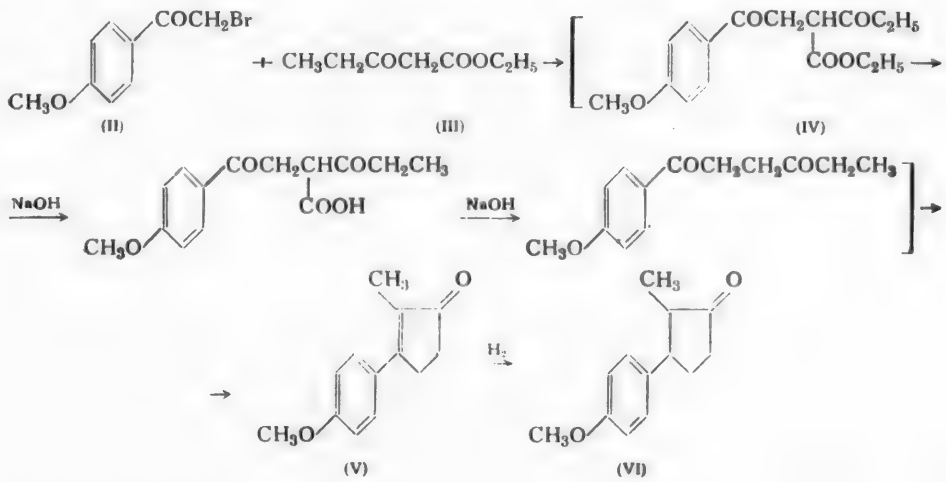
V. I. Maksimov and Z. A. Priakhina

In this paper we describe the synthesis of 3-(4-oxocyclohexyl)-2-methylcyclopentanol (I), needed by us for the preparation of analogs of steroid hormones not containing the ring C. We started with p-methoxy-



(I)

ω-bromoacetophenone (II) and ethyl propionylacetate (III), which were converted to 3-(p-methoxyphenyl)-2-methyl-2-cyclopenten-1-one (V) by the reactions based on the method for the preparation of phenylcyclopentanone-containing structures, developed by Borsche [1, 2] and by Weidlich and co-workers [3].

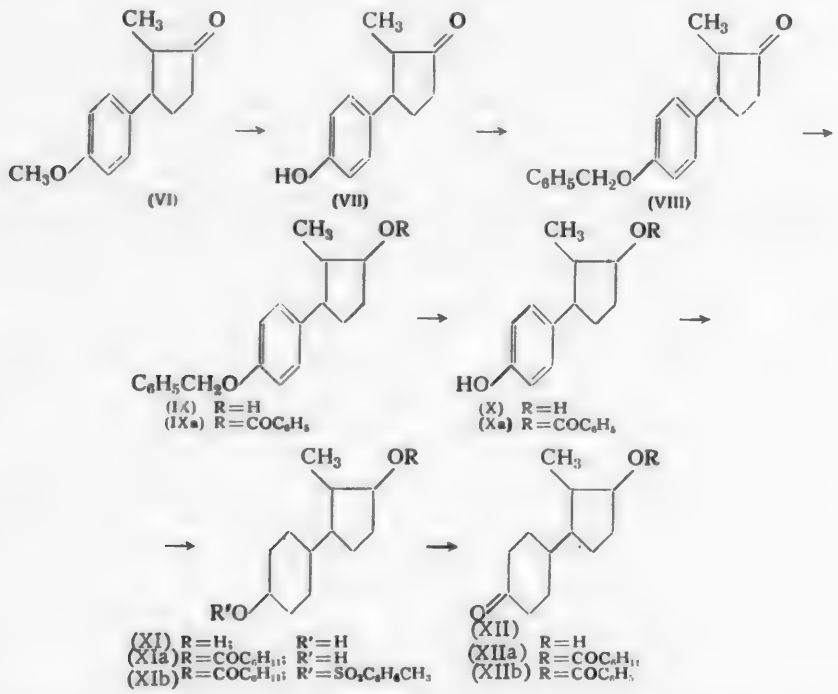


The sodio derivative of (III) was reacted with (II) in ether medium; the ethyl p-methoxyphenacylpropionylacetate (IV) without being isolated pure was subjected to saponification and ketonic cleavage by heating with 2% aqueous hydroxide solution. The resulting p-methoxyphenyl-1,4-hexanedione was immediately

converted under the influence of the alkaline medium into 3-(p-methoxyphenyl)-2-methyl-2-cyclopenten-1-one (V) [3]. The latter was isolated from the reaction mixture in a yield of 45.6%, based on (III). Its semicarbazone, the same as other unsaturated semicarbazones in this series [2, 3], assumed an intense yellow color in the light, but this color vanished when the compound was dissolved in alcohol.

The catalytic hydrogenation of the ditertiary double bond in (V) was run by us using palladium catalyst and either an acid or alkaline medium. In acid medium the hydrogen absorption went rapidly and didn't slow up after 1 mole of hydrogen had been added. The absorption stopped only after 3 moles of hydrogen had been taken up, but the obtained saturated hydrogenation product did not contain the carbonyl group. In the experiment where the reduction of (V) was terminated after the absorption of 1 mole of hydrogen we obtained a difficultly separable mixture, composed of starting substance, saturated ketone and desoxy compounds. When (V) was hydrogenated in the presence of 2% potassium hydroxide the addition of hydrogen went slowly and stopped completely after the absorption of 1 mole of hydrogen. The configuration of the 3-(p-methoxyphenyl)-2-methylcyclopentanone (VI), obtained in this manner in 95.5% yield, was not established exactly by us, but if we go by the statements of Weidlich and Meyer-Delius [4] that hydrogen adds 1,4 when α,β-unsaturated ketones are hydrogenated in alkaline medium, then the methyl group and the hydrogen at C_3 should be found in the cis-position.

The subsequent conversion of (VI) to (I) was accomplished by a series of reactions, shown in sequence in the scheme given below.



The demethylation of (VI) with a mixture of HBr and CH_3COOH gave 3-(p-hydroxyphenyl)-2-methylcyclopentanone (VII) in 89.5% yield. A temporary masking of the phenolic hydroxyl, needed for the successful carrying out of the following steps, was accomplished by converting (VII) to the benzyl ether. 3-(p-Benzyloxyphenyl)-2-methylcyclopentanone (VIII) was obtained in 79% yield by heating (VII) with benzyl chloride and potash in acetophenone medium [5]. Aluminum lithium hydride was used to reduce the keto group in (VIII); the reduction was strictly stereospecific here, since only one of the two possible epimers of 3-(p-benzyloxyphenyl)-2-methylcyclopentanol (IX) with m. p. 75.5-76° was obtained in 98% yield. By analogy with the stereospecific reduction by aluminum lithium hydride of the 17-keto group in androstane derivatives [6], and judging by the fact that the tosyl ester (XIb) is stable [7], we postulate that the hydroxyl group in (VIII) is found in the cis-position to the methyl group.

In the next step we removed the benzyl radical from the benzoate of (IX), introduced earlier to temporarily protect the phenolic hydroxyl. The debenzylation was accomplished by hydrogenating (IXa) in the presence of either Pd/$BaSO_4$ or skeletal nickel catalyst in methanol. It was observed that when the catalytic debenzylation was run with palladium catalyst at elevated temperature (40-50°), as is recommended by Morris and others [8-10], the benzoate suffered partial hydrolysis with the formation of 3-(p-hydroxyphenyl)-2-methylcyclopentanol (X).

The hydrogenation of the phenolic ring in the benzoate of 3-(p-hydroxyphenyl)-2-methylcyclopentanol was run in dioxane using as catalyst 2% Pd deposited on strontium carbonate [11]. In preliminary experiments on the reduction of ethyl p-hydroxybenzoate it was established that under our conditions the ethyl ester of p-hydroxycyclohexanecarboxylic acid is formed in quantitative yield if the hydrogenation is run at a temperature of 200-220° and a pressure of 150-160 atm. These conditions also proved suitable for the exhaustive reduction of (Xa), and the 1-hexahydrobenzoate of 3-(p-hydroxycyclohexyl)-2-methylcyclopentanol (XIa) was obtained in 97% yield as a colorless liquid with b. p. 162-163° at 0.3 mm.

A new asymmetric center arises at $C^{4'}$ in the hydrogenation of (Xa), and consequently the formation of two epimeric alcohols is possible. However, our attempts to isolate them gave a negative result—the hydrogenation was strictly stereospecific here. The tosylation of (XIa) also gave but one tosylate in quantitative yield. The latter melted at 86-87° and crystallized as completely homogeneous needles.

The oxidation of (XIa) with sodium dichromate in acetic acid [12] gave 3-(4-oxocyclohexyl)-2-methylcyclopentyl hexahydrobenzoate (XIIa) (an oil with b. p. 170-173° at 0.5 mm), which by saponification with alcoholic caustic was converted to 3-(4-oxocyclohexyl)-2-methylcyclopentanol (XII), also obtained as an oily liquid. Only its benzoate (XIIb) was obtained crystalline.

EXPERIMENTAL

p-Methoxyacetophenone was obtained by us without the use of inert solvents. To 342 g of anisole was added 280 g of aluminum chloride with stirring and cooling, and then 185 g of acetyl chloride was added in 2.5 hours at a temperature not exceeding +4°. The mixture was gradually warmed to 40°, stirred at this temperature for 3 hours, and then allowed to stand overnight. After decomposing the mixture with ice the excess anisole was vacuum-distilled on the water bath; the residue was distilled, collecting the fraction with b. p. 141-142° at 15 mm. We obtained 320 g of p-methoxyacetophenone (90.7%, based on acetyl chloride). M. p. 38°.

p-Methoxy-ω-bromoacetophenone (II). To a solution of 20 g of p-methoxyacetophenone in 70 ml of dry chloroform was added at room temperature and with stirring a solution of 21 g of bromine in 55 ml of chloroform. The reaction mixture was then slowly heated on the water bath. Hydrogen bromide began to evolve at 35°, and became quite violent at 40°; the color of the mixture changed from red-brown to light yellow, and the precipitate formed at first quickly disappeared. After the evolution of hydrogen bromide had ceased the mixture was allowed to cool; a precipitate of p-methoxy-ω-bromoacetophenone began to deposit at 28-30°. The reaction mass was washed with water. After drying the chloroform solution over calcium chloride the solvent was vacuum-distilled and the residue was recrystallized from methanol. We obtained 16.4 g of (II) with m. p. 70-71°. Yield 52%.

Ethyl propionylacetate (III) was obtained by the Blaise method [13, 14]; the reaction of ethylmagnesium bromide with ethyl cyanoacetate was run at a temperature not exceeding 20°.

Ethyl p-methoxyphenacylpropionylacetate (IV). To 1.8 g of sodium dust in 100 ml of ether was added with stirring in 1.5 hours a solution of 10 g of ethyl propionylacetate in 50 ml of ether and the mixture was then heated for 3 hours until all of the sodium had dissolved. The obtained sodio derivative was then treated in 40 minutes with a solution of 15.9 g of p-methoxy-ω-bromoacetophenone in 150 ml of ether. The yellow-colored reaction mixture was heated for 7 hours, and then with external cooling was treated with 40 ml of water. The ether layer was separated and after the usual treatment of the extract* we obtained 20 g of p-methoxyphenacylpropionylacetic ester (IV) as a viscous oil. It was used without further purification for the preparation of (V).

*The "usual treatment" of extracts in an organic solvent consists in their being washed, dried, and the solvent removed by distillation.

3-(p-Methoxyphenyl)-2-methyl-2-cyclopenten-1-one (V). A mixture of 20 g of crude ethyl p-methoxyphenacylpropionylacetate and 800 ml of 2% sodium hydroxide solution was heated with stirring at 40-50° for 6 hours, at which time the ester gradually went into solution. Then the mixture was rapidly brought to the boil and boiled for 10 minutes. The oily layer that separated on cooling was extracted with ether, the ether extract was subjected to the usual treatment, and the residue (V) distilled at 142-145° at 1 mm as a colorless oil, which crystallized in the receiver. Yield 6.4 g (45.6%). M. p. 61-62° (from ethyl acetate).

Found %: C 76.97, 77.06; H 7.16, 6.81. $C_{13}H_{14}O_2$. Calculated %: C 77.2; H 6.97.

The semicarbazone with m. p. 238-239° (with decompn.) rapidly turns yellow in the light; a colorless solution is obtained when the colored compound is dissolved in alcohol.

Found %: N 16.31. $C_{14}H_{17}O_2N_3$. Calculated %: N 16.21.

3-(p-Methoxyphenyl)-2-methylcyclopentanone (VI). Ten grams of (V) was hydrogenated with 20 g of previously reduced 2% $Pd/CaCO_3$ in 300 ml of methanol, containing 0.2 g of potassium hydroxide; 1 mole of hydrogen was absorbed in 6 hours. The catalyst was filtered, the filtrate neutralized with acetic acid, the solvent distilled off, and the residue vacuum distilled. We obtained 9.55 g of highly viscous oil; b. p. 115-116° at 2 mm, n_D^{20} 1.542.

Found %: C 76.64, 76.97; H 7.94, 7.96. $C_{13}H_{16}O_2$. Calculated %: C 76.44; H 7.89.

The semicarbazone of (VI) with m. p. 217.5-218.5° does not change in the light.

Found %: C 64.39, 64.31; H 7.42, 7.21; N 16.16. $C_{14}H_{19}O_2N_3$. Calculated %: C 64.34; H 7.33; N 16.08.

3-(p-Hydroxyphenyl)-2-methylcyclopentanone (VII). A solution of 14 g of (VI) in a mixture of 280 ml of glacial acetic acid and 280 ml of hydrobromic acid (d 1.46) was refluxed in a carbon dioxide stream for 2.5 hours, after which the acetic and hydrobromic acids were removed by vacuum-distillation. The residue was dissolved in 5% sodium hydroxide solution; the obtained solution was extracted with ether and then acidified with hydrochloric acid until acid to Congo. The separated crystals were filtered and recrystallized from either ethyl acetate or 50% aqueous alcohol. We obtained 11.65 g (89.5%) of 3-(p-hydroxyphenyl)-2-methylcyclopentanone with m. p. 138-139°.

Found %: C 75.60, 75.82; H 7.47, 7.39. $C_{12}H_{14}O_2$. Calculated %: C 75.80; H 7.36.

3-(p-Benzyloxyphenyl)-2-methylcyclopentanone (VIII). A solution of 20 g of (VII) in 100 ml of acetophenone was treated at 100° with 18 g of finely divided potash and then at 140° in drops with 16.5 g of benzyl chloride. After heating at the latter temperature for 7 hours the excess benzyl chloride and the acetophenone were steam-distilled. The oily residue was rubbed with 2% potassium hydroxide solution and then recrystallized from 80% alcohol. M. p. 79-79.7°. Yield 79.4%.

Found %: C 80.92; H 7.05. $C_{19}H_{20}O_2$. Calculated %: C 81.03; H 7.19.

3-(p-Benzyloxyphenyl)-2-methylcyclopentanol (IX). To a suspension of 1.6 g of aluminum lithium hydride in 60 ml of absolute ether was added with stirring 10 g of (VIII) in 100 ml of absolute ether at such a rate that the reaction mass refluxed. The mixture was refluxed for 1 hour and then with external cooling by ice it was treated with water in drops (to decompose the excess aluminum lithium hydride) and hydrochloric acid until all of the precipitate had dissolved. The separated ether layer was subjected to the usual treatment; removal of the solvent gave 9.8 g of 3-(p-benzyloxyphenyl)-2-methylcyclopentanol with m. p. 73-74°. For analysis the substance was recrystallized from a mixture of benzene and benzine. M. p. 75.5-76°.

Found %: C 81.02, 80.89; H 8.11, 8.00. $C_{19}H_{22}O_2$. Calculated %: C 81.04; H 7.91.

3-(p-Benzloxyphenyl)-2-methylcyclopentyl benzoate (IXa) was obtained by reacting 9.5 g of (IX) with 6.5 g of benzoyl chloride in a mixture of 35 ml of dioxane and 13 ml of pyridine at room temperature. The obtained yellow oily product (12.5 g) was dissolved in 50 ml of benzene and then passed through a column containing aluminum oxide, which was then eluted with benzene. After vacuum-distillation of the solvent the residue crystallized. Recrystallized from a mixture of benzene and benzine, the substance had m. p. 70.5-71.5°.

Found %: C 81.23; H 6.74. $C_{26}H_{26}O_3$. Calculated %: C 80.9; H 6.78.

3-(p-Hydroxyphenyl)-2-methylcyclopentyl benzoate (Xa) (debenzylation). a) A solution of 3 g of (IXa) in 150 ml of methanol was hydrogenated with 3 g of 2.5% palladinized barium sulfate. When the hydrogen absorption slowed up another 2 g of catalyst was added and the hydrogenation continued until the calculated amount of hydrogen had been absorbed (6.5 hours). After removal of the catalyst and vacuum distillation (30°) of the solvent the residue (m. p. 107.5-109°) was recrystallized from a mixture of benzene and benzine. Yield 93%.

Found %: C 76.8; H 6.74. $C_{19}H_{20}O_3$. Calculated %: C 77.06; H 6.78.

The hydrogenation of (IXa) at 40° gave a mixture which after treatment with sodium bicarbonate and subsequent acidification yielded benzoic acid with m. p. 119-121° (identified by mixed melting point). In addition, recrystallization from a mixture of benzene and benzine gave two compounds with m. p. 108.8-109.5° (Xa) and with m. p. 147.3-147.7°; based on its analysis the latter is 3-(p-hydroxyphenyl)-2-methylcyclopentanol (X).

Found %: C 75.26, 74.83; H 8.04, 8.25. $C_{12}H_{16}O_2$. Calculated %: C 74.96; H 8.39.

b) To a suspension of 1 g of skeletal nickel catalyst in 40 ml of methanol, previously saturated with hydrogen, was added a solution of 0.5 g of (IXa) in 30 ml of methanol, and the whole hydrogenated at atmospheric pressure. The amount of hydrogen absorbed in 25 minutes was 35 ml (compared to theoretical 32 ml). We obtained 0.38 g of (Xa) with m. p. 107-108°.

3-(p-Hydroxycyclohexyl)-2-methylcyclopentyl hexahydrobenzoate (XIa). Into a stainless steel autoclave fitted with stirrer was placed 10 g of benzoate (Xa), 5 g of 2% $Pd/SrCO_3$ catalyst and 300 g of peroxide-free dioxane. After removal of air the autoclave was filled with hydrogen to a pressure of 110-120 atm, then gradually heated to 200-220° and kept at this temperature for 2 hours. Here the pressure in the autoclave rose to 150-160 atm, while the residual pressure in the autoclave after its cooling was 90 atm. After distilling off the solvent the obtained residue (viscous colorless oil) was vacuum-distilled; b. p. 162-163° at 0.3 mm. Yield 9.7 g.

Found %: C 73.9, 74.08; H 10.55, 10.39. $C_{19}H_{32}O_3$. Calculated %: C 74.04; H 10.31.

(XIb) Tosylate, m. p. 86-87°.

Found %: C 67.46; H 8.35; S 6.99. $C_{26}H_{38}O_5S$. Calculated %: C 67.49; H 8.28; S 6.93.

3-(4-Oxocyclohexyl)-2-methylcyclopentyl hexahydrobenzoate (XIIa). A solution of 2 g of (XIa) in 20 ml of glacial acetic acid (stable to CrO_3) was treated with a solution of 0.7 g of sodium dichromate in 7 ml of acetic acid; the temperature was kept at 20°. The mixture was stirred for another hour and then allowed to stand for 12 hours. The reaction mass was diluted with 100 ml of water and the acetic acid and part of the water were vacuum-distilled. The residue was diluted with water and then extracted with ether. After the usual treatment of the ether extract the residue was vacuum-distilled. We obtained 1.85 g (92.5%) of a noncrystallizing oil with b. p. 170-173° at 0.4 mm.

Found %: C 74.30; H 9.81. $C_{19}H_{30}O_3$. Calculated %: C 74.07; H 9.81.

(XIIa) Semicarbazone, m. p. 167-168°.

Found %: C 66.10; H 9.23; N 11.65. $C_{20}H_{33}O_3N_3$. Calculated %: C 66.08; H 9.15; N 11.56.

3-(4-Oxocyclohexyl)-2-methylcyclopentanol (XII) was obtained by saponifying its hexahydrobenzoate with methanolic potassium hydroxide with heating for 2.5 hours. The methanol was then vacuum-distilled, and the residue was diluted with water and extracted with ether. After the usual treatment we obtained 3.65 g of yellowish oily substance. To purify the substance its chloroform solution was passed through a column containing aluminum oxide, from which (XII) was eluted using 500 ml of chloroform. Removal of the chloroform by distillation (at the end in vacuo) left a colorless oil.

Found %: C 73.34, 73.50; H 10.31, 10.57. $C_{12}H_{20}O_2$. Calculated %: C 73.43; H 10.22.

3-(4-Oxocyclohexyl)-2-methylcyclopentyl benzoate (XIIb). A solution of 2.85 g of (XII) in 15 ml of pyridine was treated at 20° with 2.4 g of benzoyl chloride. The next day the reaction mass was poured into water, acidified with hydrochloric acid until acid to Congo, and stirred for 2 hours. The obtained precipitate was filtered, washed with water, then with sodium bicarbonate solution, again with water, dried in a vacuum-desiccator, rubbed with a small amount of hexane to remove oily impurities, and finally recrystallized from 70% ethanol. We obtained 3.66 g (84%) of the benzoate with m. p. 76-76.5°.

Found %: C 76.20; H 8.07. $C_{19}H_{24}O_3$. Calculated %: C 75.96; H 8.07.

The semicarbazone of the benzoate has m. p. 163-164° (with decompn.; from alcohol).

SUMMARY

Starting with p-methoxyacetophenone and ethyl propionylacetate we synthesized 3-(4-oxocyclohexyl)-2-methylcyclopentanol.

LITERATURE CITED

[1] W. Borsche and W. Menz, Ber. 41, 190 (1908).

[2] W. Borsche and A. Fels, Ber. 39, 1922 (1906).

[3] H. Weidlich and G. Daniels, Ber. 72, 1590 (1939).

[4] H. Weidlich and M. Meyer-Delius, Ber. 72, 1941 (1939).

[5] R. O. Clinton and T. A. Geissman, J. Am. Chem. Soc. 65, 85 (1943).

[6] U. S. Patent 2,588,294 (1952); Ch. A. 46, 9628e (1952).

[7] O. S. Madaeva and F. A. Lur'i, Proc. Acad. Sci. USSR 84, 713 (1952).

[8] S. Morris, J. Am. Chem. Soc. 71, 2056 (1949).

[9] S. Morris and R. Riemenschneider, J. Am. Chem. Soc. 68, 500 (1946).

[10] K. Merz and W. Hagemann, Arch. Pharm. 282, 79 (1943).

[11] R. Martin and R. Robinson, J. Chem. Soc. 1943, 491.

[12] L. Fieser and H. Heymann, J. Am. Chem. Soc. 73, 5858 (1951).

[13] E. Blaise, Compt. rend. 132, 978 (1901).

[14] R. Willstätter and C. Clarke, Ber. 47, 298 (1914).

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ANALOGS OF STEROID HORMONES

II. SYNTHESIS OF 6-(2-METHYL-3-HYDROXYPENTYL)-$\Delta^{1(9)}$-OCTALONE

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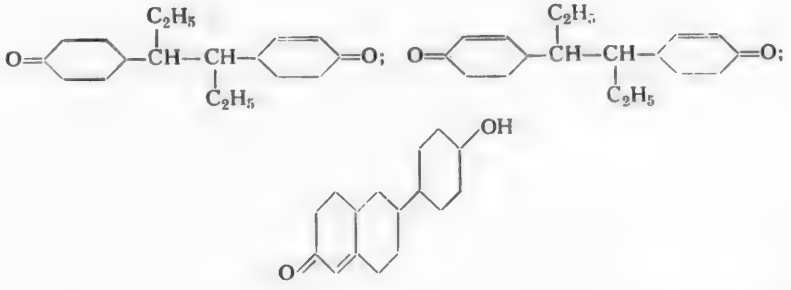
Extensive investigations made in the field of analogs of follicular hormones have revealed that there exists a large number of compounds, lacking the steroid structure, but possessing all of the physiological properties of the natural hormones. Many of these so-called "synthetic estrogens" have a physiological activity that equals or even exceeds the activity of the natural hormones; some of them, as for example diethylstilbestrol, have found wide application in clinical practice.

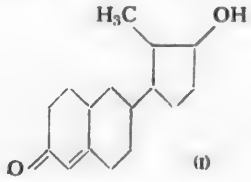
In contrast to this, studies devoted to a search for analogs of other steroid hormones have not received sufficient development. For example, until now, only several nonsteroid compounds have been described which have proved capable of showing to variable degree the physiological reactions characteristic for the male sex hormone. Included among them are 3-(oxocyclohexyl)-4-(oxocyclohexenyl)hexane, 3,4-di-(4-oxocyclohexenyl)-hexane [1], 6-(4'-hydroxycyclohexyl)-$\Delta^{1(9)}$-2-octalone [2, 3], and some compounds analogous to the latter.



These examples indicate that the androgenic activity is apparently not strictly specific, and that it is linked only with the androstane and perhydrochrysene (the so-called D-homosteroids) structures.

In order to make further systematic searches for analogs of the steroid hormones it is necessary to have additional information on the relationship between physiological properties and structure, and in particular to know to what extent changes in the skeleton of steroid hormones are permissible.

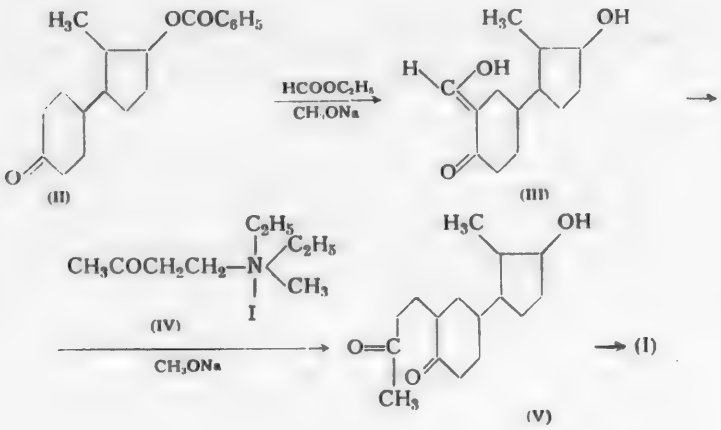
In connection with this we made a study of the synthesis of 6-(2-methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone (I). It is possible to regard this compound as being an analog of the androgenic hormones, lacking the ring C and the angular methyl group at C_{10}.



(I)

Based on the examples of 19-nortestosterone [4], 19-norprogesterone [5] and 19-nordesoxycorticosterone [6], it is known that an angular methyl group between rings A and B is not essential for the appearance of the corresponding hormonal activity.

6-(2-Methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone (I) was obtained from the earlier synthesized [7] benzoate of 3-(4-oxocyclohexyl)-2-methylpentanol (II). To convert (II) to the octalone derivative we used the method of Robinson and co-workers [8], widely used in recent years for introducing into cyclic ketones a new cycle, containing a keto group with a conjugated double bond. The method consists of the condensation of the starting ketone with methyl vinyl ketone in the presence of a base, followed by closure of the formed diketone into a new cycle on the type of a crotonic condensation. Instead of the unstable and easily polymerized methyl vinyl ketone it is also possible to use diethylamino-2-butanone methiodide (IV) in this reaction, which under the conditions of the condensation reaction is converted into methyl vinyl ketone. Since it is known [8] that the introduction of a formyl radical in the α-position to the keto group facilitates the addition of methyl vinyl ketone, we first converted (II) to its formyl derivative (III), which was then condensed with (IV).



The reaction of (II) with ethyl formate was run in benzene in the presence of sodium methylate. The formation of (III) was accompanied by a side transesterification reaction, since ethyl benzoate was isolated from the reaction mixture. The obtained 3-(3-hydroxymethylene-4-oxocyclohexyl)-2-methyl-1-cyclopentanol (III) showed an absorption maximum in the UV region (λ_{max} 281 mμ) characteristic for the formyl grouping [9], and gave an intense violet color with ferric chloride.

The reaction of (III) with (IV) in the presence of sodium methylate gave 3-[3-(γ-oxobutyl)-4-oxocyclohexyl]-2-methylcyclopentanol (V). To cyclize (V) we used potassium hydroxide in methanol solution at room temperature. The oily substance isolated from the reaction mixture was purified by chromatographing on aluminum oxide, followed by recrystallization from ether. 6-(2-Methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone (I) crystallized as slender needles with m. p. 107.5-109.5°. It shows an absorption maximum at 238 mμ. Its p-nitrobenzoate has m. p. 106-108°.

The biological testing of 6-(2-methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone, done by I. N. Lektorskii (Pharmacology Section of the All-Union Chemical Pharmaceutical Research Institute), revealed that it is inactive in dosage up to 7 mg when tested for comb-growth on roosters.

EXPERIMENTAL

3-(3-Hydroxymethylene-4-oxocyclohexyl)-2-methyl-1-cyclopentanol (III). To a suspension of sodium methylate (from 0.3 g of sodium) in 7 ml of benzene was added in a stream of nitrogen at room temperature with stirring 7.5 g of ethyl formate in drops. After the sodium methylate had dissolved, to the yellow reaction

mass with ice-cooling was added a solution of 1 g of 3-(4-oxocyclohexyl)-2-methyl-1-cyclopentanol benzoate in 6 ml of benzene, and the mixture was stirred for 20 hours. The resulting formyl compound was repeatedly extracted with 2% sodium hydroxide solution. The alkaline extracts were treated with ether and then acidified with hydrochloric acid until acid to Congo. The obtained oily substance was extracted with chloroform. After treating the chloroform extract in the usual manner the solvent was vacuum-distilled in a nitrogen stream at a bath temperature not exceeding 30°. We obtained 0.75 g of residue as a yellow oil. The oil gives an intense violet color with ferric chloride and has λ_{max} 281 mμ in the ultraviolet region. This substance was used without further purification in the next step.

The oily residue, obtained in an amount of 0.35 g after distilling off the solvents from the combined benzene solution and ether extract, distilled at 222°. Its saponification with methanolic potassium hydroxide solution gave benzoic acid (m. p. 119-120°).

3-[3-(γ-Oxobutyl)-4-oxocyclohexyl]-2-methyl-1-cyclopentanol (V). To a solution of sodium methylate (from 0.2 g of sodium and 7.5 ml of methanol) in a stream of nitrogen was added a solution of 0.75 g of (III) in 7 ml of methanol, and the mixture stirred for 30 minutes at room temperature. Then the mixture was cooled in an ice-salt mixture and treated in drops with a solution of diethylamino-2-butanone methiodide (from 1.3 g of diethylamino-2-butanone and 2 g of methyl iodide) in 5 ml of methanol. After stirring for 15 minutes the cooling bath was removed and the reaction mass was allowed to stand at room temperature for 18 hours. Then with cooling it was acidified with 10% hydrochloric acid, diluted with water, and extracted with chloroform. After the usual treatment of the chloroform extract and removal of the solvent by distillation we obtained 0.85 g of an oily residue, containing 3-[3-(γ-oxobutyl)-4-oxocyclohexyl]-2-methylcyclopentanol (does not react to color test with ferric chloride). It was used without purification in the subsequent reactions.

6-(2-Methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone. A mixture of 0.5 g of (V), 2 g of potassium hydroxide and 50 ml of methanol was stirred for 2.5 hours at room temperature. Then the reaction mass was cooled, carefully neutralized with dilute hydrochloric acid, and the mixture extracted with chloroform. The chloroform extract was washed with water, and then dried over anhydrous sodium sulfate. After distilling off the chloroform (at the end in vacuo) we obtained 0.45 g of a yellow oily residue, having λ_{max} 238 mμ in the UV region. This residue was dissolved in 10 ml of dry benzene and the solution passed through a column containing neutral aluminum oxide, diluted with ethyl acetate. The crystalline fractions, obtained on washing the column with a mixture of benzene and ether (1 : 1), were combined and purified by recrystallization from ether. The 6-(2-methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone was obtained as needles with m. p. 107.5-109°; λ_{max} 238 mμ log E 4.20.

Found %: C 77.23; H 9.71. $C_{16}H_{24}O_2$. Calculated %: C 77.37; H 9.72.

6-(2-Methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone p-nitrobenzoate. To a solution of 0.2 g of the oily substance, obtained after cyclization, in 3 ml of dry pyridine was added with ice-water cooling 0.19 g of p-nitrobenzoyl chloride. The next day the reaction mixture was poured into water and stirred for 1.5 hours. The obtained oily substance was extracted with ether. The ether extract was washed with water, dilute hydrochloric acid, soda solution, again with water, and then dried over sodium sulfate. Removal of the ether by distillation left 0.27 g of oily substance, which crystallized on standing. Two recrystallizations from ether gave 6-(2-methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone p-nitrobenzoate with m. p. 106-108°.

Found %: C 69.62; H 6.79. $C_{23}H_{27}O_5N$. Calculated %: C 69.5; H 6.85.

SUMMARY

6-(2-Methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone was synthesized from 3-(4-oxocyclohexyl)-2-methylpentanol.

LITERATURE CITED

[1] H. E. Ungnade and P. W. Tucker, J. Am. Chem. Soc. 71, 1381 (1949).

[2] A. L. Wilds, C. H. Shunk and H. Hoffman, J. Am. Chem. Soc. 71, 3266 (1949).

[3] A. L. Wilds, C. H. Hoffman and T. H. Pearson, J. Am. Chem. Soc. 77, 647 (1955).

[4] A. J. Birch, J. Chem. Soc. 1950, 367.

[5] C. Djerassi et al., J. Am. Chem. Soc. 73, 3540 (1951).

[6] A. Sandoval et al., J. Am. Chem. Soc. 75, 4117 (1953).

[7] V. I. Maksimov and Z. A. Priakhina, J. Gen. Chem. 28, 252 (1958). •

[8] E. C. du Feu, F. J. McQuillin and R. Robinson, J. Chem. Soc. 1937, 53.

[9] A. L. Wilds and C. H. Shunk, J. Am. Chem. Soc. 71, 3946 (1949).

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ALKALOIDS OF SALSOLA RICHTERI

VI. STRUCTURE OF SALSAMINE

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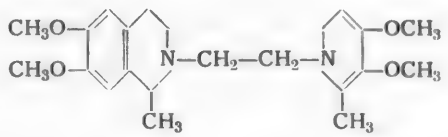
In an earlier paper we had described the isolation of the alkaloid salsamine from the above-ground portions of the Central Asiatic plant Salsola Richteri, the analysis of which gave values lying between those calculated for the formulas $C_{12}H_{17}O_2N$ and $C_{13}H_{19}O_2N$ [1]. In this paper we give the results of a more detailed study of salsamine. It was established that this base when purified more carefully is optically inactive and had m. p. 165-167°. Based on its analysis and determination of the molecular weight (428) this substance should be assigned the formula $C_{28}H_{36}O_4N_2$. All four oxygen atoms in salsamine are found present as methoxy groups. In addition to salsamine, we also isolated optically active base, isomeric with salsamine, from the mother liquors.

The oxidation of salsamine and of its optically active isomer with permanganate gave the same optically inactive oxidation product having a neutral character ($C_{24}H_{28}O_6N_2$). The composition and properties of this latter substance show that the oxidation of salsamine proceeds with the cleavage of two carbon atoms and the formation of lactam groups similar to what occurs in the oxidation of salsolidine under the same conditions [2]. On this basis it can be postulated that salsamine and its isomer are the respective condensation products of dl-salsolidine and l-salsolidine with dichloroethane, which was confirmed experimentally. The condensation of dl-salsolidine with dichloroethane gave a base identical with salsamine, while the condensation of l-salsolidine with dichloroethane gave the dextrorotatory base isomeric with salsamine. Both bases can be depicted by the formula given below.



Consequently, both salsamine and its optically active isomer are apparently not found as such in the plant, but are formed in the process of extracting the alkaloids from the plant with dichloroethane.

EXPERIMENTAL

The earlier described procedure [1] was used to isolate salsamine from the mother liquors of the total alkaloids found in Salsola Richteri. The separation of salsamine and its optically active isomer was effected on the basis of the different solubility of their hydrochlorides. When a mixture of the hydrochlorides is recrystallized from alcohol the first to crystallize is the more difficultly soluble salsamine hydrochloride, which after purification has m. p. 242-247°. Evaporation of the mother liquors to small volume gave an amorphous hydrochloride, which after boiling with acetone was dissolved in alcohol. Dilution of the alcohol solution with 10 volumes of acetone, followed by standing, gave a powder-like crystalline precipitate. After the hydrochloride was purified by recrystallization from alcohol it had m. p. 196-198°. The free base isolated from the hydrochloride, after recrystallization from acetone, had m. p. 96-98° and $[\alpha]_D$ +37.5° (c 2.0, in alcohol).

Found %: C 71.03; H 8.19; N 6.43; CH_3O 27.4. $C_{26}H_{36}O_4N_2$. Calculated %: C 70.90; H 8.18; N 6.36; $4CH_3O$ 28.1.

Oxidation of salsamine with permanganate in acetone solution. To a solution of 0.5 g of salsamine with m. p. 165-167° in 50 ml of acetone was added in drops an acetone solution of $KMnO_4$ (0.92 g in 100 ml). The MnO_2 precipitate was filtered and washed with acetone. The acetone solution was reduced to a small volume. The obtained precipitate of oxidation product was recrystallized from alcohol (m. p. 212-214°).

Found %: C 65.21; H 6.29; N 6.47. $C_{24}H_{28}O_5N_2$. Calculated %: C 65.45; H 6.36; N 6.36.

Oxidation of isomer of salsamine with permanganate in acetone solution. The base (0.5 g) with m. p. 96-98° and $[\alpha]_D$ +37.5° was oxidized with permanganate under the conditions of the preceding experiment. A mixture of the isolated oxidation product (m. p. 212-214°) with the oxidation product of salsamine did not depress the melting point.

Condensation of dl-salsolidine with dichloroethane. A solution of 2 g of dl-salsolidine with m. p. 52-53° in 50 ml of dichloroethane was refluxed in the presence of 2 g of $NaHCO_3$ for 8 hours. The filtered solution was vacuum-distilled to dryness, the residue dissolved in 5% hydrochloric acid, the solution filtered, and the free base isolated by the addition of $NaHCO_3$ and subsequent extraction with ether. After we distilled off the ether the crystalline residue was boiled with acetone, and then recrystallized several times from alcohol (m. p. 165-167°). Its mixture with salsamine did not depress the melting point.

Found %: C 70.75; H 8.20; N 6.52. $C_{26}H_{36}O_4N_2$. Calculated %: C 70.90; H 8.18; N 6.36.

The hydrochloride of the condensation product obtained from dl-salsolidine had m. p. 242-247°.

Condensation of l-salsolidine with dichloroethane. Two grams of l-salsolidine with m. p. 57-60° and $[\alpha]_D$ −59.7° was condensed with dichloroethane under the conditions of the preceding experiment. After the base was purified by recrystallization from alcohol it had m. p. 96-98° and $[\alpha]_D$ +37.5° (c 2.0, in alcohol).

The hydrochloride of the condensation product of l-salsolidine with dichloroethane was obtained as an amorphous mass by treating the free base with alcoholic hydrochloric acid. Dissolving the amorphous hydrochloride in a small amount of alcohol, followed by dilution with acetone, gave the crystalline hydrochloride (m. p. 196-198°).

SUMMARY

1. After isolating the main alkaloids of Salsola Richteri, still another new base, isomeric with salsamine, was isolated from the mother liquors.

2. The condensation of dl-salsolidine and of l-salsolidine with dichloroethane gave respectively salsamine and its optically active isomer.

LITERATURE CITED

[1] N. F. Proskurnina and A. P. Orekhov, J. Gen. Chem. 7, 1999 (1937).

[2] N. F. Proskurnina and A. P. Orekhov, J. Gen. Chem. 10, 707 (1940).

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ACONITE ALKALOIDS

IX. ALKALOIDS OF ACONITUM EXCELSUM

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The alkaloids of the tall aconite (Aconitum excelsum Rehb.) were studied by S. Iu. Iunosov, who briefly mentioned in his paper [1] the isolation of mesaconitine and two bases, characterized only by their melting points (265-267°, and about 100°).

We investigated the roots of the tall aconite. The material was collected in T'ien-Shang in the fall after the above-ground portion of the plant had withered. The investigated sample contained 3% of mixed alkaloids, the paper-chromatographing of which showed the presence of only three substances (R_f 0.66, 0.49 and 0.38). Separation of the mixture permitted isolating lappaconitine (R_f 0.66) and two new alkaloids (R_f 0.74 and 0.76), which were not found when the total alkaloids were chromatographed on paper and for which we propose the name of acsine and acsinatine. The dry roots were shown to contain 1.6% lappaconitine, 0.016% acsine and 0.002% acsinatine. Consequently, the investigated material contained at least five bases. The substances, having R_f 0.49 and 0.38, could not be isolated in the pure state.

Acsine, $C_{21}H_{29}O_5N$, contains two alcoholic OH groups, one acetoxy group, and apparently an ether linkage. Acsinatine, $C_{21}H_{27}O_4N$, contains one alcoholic OH group, one keto group, and the same as acsine, one acetoxy group. Saponification of the acetoxy groups from acsine and acsinatine gave amino alcohols, respectively acsinidine, $C_{19}H_{27}O_4N$, and acsinatidine, $C_{19}H_{25}O_3N$.

The above-ground portions of the tall aconite, collected in T'ien-Shang in the preflowering stage, contained 0.5% of noncrystalline total alkaloids; the chromatographing of the total alkaloids on paper revealed the presence of three substances (R_f 0.64, 0.49 and 0.38). We were able to isolate only lappaconitine (0.06%) from this mixture of substances.

EXPERIMENTAL

Isolation of Alkaloids

Forty-five kilograms of dried and ground roots of Aconitum excelsum was moistened with 5% soda solution and then exhaustively extracted with dichloroethane. The alkaloids were extracted from the dichloroethane solution with 5% H_2SO_4. The sulfuric acid extract was treated with a small amount of ether; then the mixture with vigorous shaking was made alkaline with 5% soda solution. The crystalline precipitate (1025 g, portion A) was filtered; extraction of the filtrate with ether yielded 357 g of an oily mixture of bases (portion B). When chromatographed on Leningrad Factory No. 2 paper (solvent—butanol, saturated 5% CH_3COOH, temperature around 20°, developer-Dragendorff's reagent) portion A was shown to contain one substance (R_f 0.66) while portion B was found to contain three substances (R_f 0.66, 0.49 and 0.38).

The mixture of crystalline bases (portion A) (1025 g) was dissolved in 6 liters of 5% hydrochloric acid and the solution treated with an excess of saturated $NaClO_4$ solution. The perchlorate precipitate, obtained as an oil, was separated from the aqueous solution, washed with a small amount of water, and then dissolved with heating in 2 liters of CH_3OH. The crystalline precipitate of lappaconitine perchlorate obtained on cooling was purified by refluxing with 1 liter of CH_3OH; yield 800 g, m. p. 250°. The lappaconitine was identified by its direct comparison with the lappaconitine obtained from Aconitum oriental [2]. After removal and

purification of the lappaconitine perchlorate, the aqueous and methanolic solutions were worked up to yield 315 g of an oily mixture of bases, which were separated by their basicity into 18 fractions. When chromatographed on paper, all of the fractions were found to contain only lappaconitine (R_f 0.66), and here 80 g of it was isolated.

The tarry mixture of alkaloids (portion B) (357 g) was dissolved in 400 ml of 5% H_2SO_4; fractional alkalization with 19 equal portions of caustic and extraction with ether gave 19 fractions. After rubbing these with ether we were able to isolate 5.5 g of lappaconitine from fractions 9-14, and 6.5 g of acsine from fractions 15-18. From the ether mother liquors after removal of the acsine a second division of the alkaloids by basicity into 10 fractions yielded 0.5 g of acsine and 1.2 g of acsinatine. From the 19th fraction after a second division of the alkaloids by basicity we isolated 1.9 g of the difficultly water-soluble acsine sulfate and 0.3 g of acsinatine.

When heated slowly acsine melts at 182-185°, and when heated rapidly it melts at 192-195°; it is difficultly soluble in ether, acetone and alcohol, and somewhat more soluble in chloroform; R_f 0.74 $[\alpha]_D^{20}$ +4.2° (c 10.0, CH_3OH). Its infrared spectrum shows bands at 3704 cm^{-1} and 3333 cm^{-1} (OH groups), while in the 1650-1750 region only one band is found at 1737 cm^{-1} (ester carbonyl).

Found %: C 66.90, 66.50; H 8.14, 7.90; N 3.70, 3.58; OH 8.66. $C_{21}H_{29}O_5N$. Calculated %: C 67.18; H 7.78; N 3.73; OH 9.05.

Acsine sulfate was obtained by treating the free base with 5% H_2SO_4, m. p. 220° (decompn.).

Found %: C 59.76, 59.31; H 7.00, 6.99; N 3.38; S 3.73. $C_{21}H_{29}O_5N \cdot H_2SO_4$. Calculated %: C 59.41; H 7.12; N 3.30; S 3.77.

Acsinatine melts at 246-247°, R_f 0.76, is difficultly soluble in ether, alcohol and acetone, and readily soluble in chloroform; it fails to give crystalline salts with the common organic and inorganic acids. Its infrared spectrum shows bands at 3704 cm^{-1} (OH), 1737 cm^{-1} (ester carbonyl) and 1724 cm^{-1} (keto group).

Found %: C 70.99, 70.90; H 7.59, 7.65; N 4.06, 4.29; OH 5.04. $C_{21}H_{27}O_4N$. Calculated %: C 70.57; H 7.61; N 3.91; OH 4.74.

Saponification of Acsine and Acsinatine

A solution of 0.5 g of acsine and 0.4 g of NaOH in 20 ml of CH_3OH was refluxed for 1 hour. The residue after removal of the alcohol was dissolved in 5 ml of water. Extraction with chloroform gave 0.3 g of oily substance, which crystallized when rubbed with acetone. We obtained 0.1 g of acsinidine, m. p. 248-249.5° (from aqueous acetone).

Found %: C 68.60, 68.03; H 8.13, 7.84; N 4.07, 3.76. $C_{19}H_{27}O_4N$. Calculated %: C 67.44; H 8.16; N 4.29.

From 0.5 g of acsinatine, after saponification and treatment in the same manner as described above, we obtained 0.15 g of acsinatidine, m. p. 225-227° (from aqueous acetone).

Found %: C 72.24, 71.79; H 8.31, 8.31; N 3.92, 3.82. $C_{19}H_{25}O_3N$. Calculated %: C 72.35; H 7.98; N 4.44.

Acsinatidine hydrochloride was obtained by mixing alcohol solutions of the free base and hydrogen chloride. The addition of ether gave a crystalline precipitate, m. p. 284-285°.

SUMMARY

From the tall aconite (Aconitum excelsum Rehb.) we isolated lappaconitine and two new alkaloids—acsine, $C_{21}H_{29}O_5N$, and acsinatine, $C_{21}H_{27}O_4N$.

LITERATURE CITED

[1] S. Iu. Iunusov, J. Gen. Chem. 18, 513 (1948).

[2] A. D. Kuzovkov and P. S. Massagetov, J. Gen. Chem. 25, 178 (1955).*

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ELECTROLYTIC REDUCTION OF 2,4-DIAMINO-5-ISONITROSO-6-HYDROXYPYRIMIDINE

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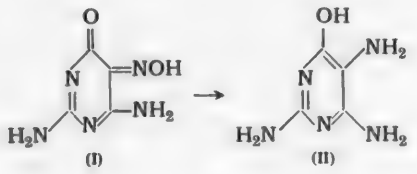
The chemical and catalytic reduction of nitroso groups in pyridine compounds has been discussed in considerable detail in the literature, in particular for 2,4-diamino-5-isonitroso-6-hydroxypyrimidine [1, 2], which has importance in the synthesis of folic acid. However the method of electrolytic reduction of nitrosopyrimidines has been studied but slightly. Among the few studies in this field, mention should be made of the electroreduction of 3-methyl-4-amino-5-isonitroso-2,6-dihydroxypyrimidine at a lead cathode in 60% sulfuric acid [3].

In this paper we studied the electrolytic reduction of 2,4-diamino-5-isonitroso-6-hydroxypyrimidine (I) in both acid and alkaline media; the yield of 2,4,5-triamino-6-hydroxypyrimidine (II) was 77-80%.



The reduction of aromatic nitroso compounds usually proceeds in higher yield (93-97%) [4-6].

EXPERIMENTAL

The apparatus used for the reduction was a diaphragmed porcelain beaker, containing the cathode as a perforated metal cylinder or spiral tube, a coil for cooling, and a stirrer. In the anodic section was placed either a lead or a nickel anode (the first for acid, and the second for alkaline reduction), and it was filled with either 10% sulfuric acid or 10% sodium hydroxide solution.

In acid medium the electroreduction of 10 g of a suspension of 2,4-diamino-5-isonitroso-6-hydroxypyrimidine was run with stirring in a 250 ml diaphragmed beaker containing 150 ml of hydrochloric acid solution (of variable concentration). On conclusion of reduction the solution was filtered, evaporated in vacuo to a volume of 80 ml, diluted with water to 250 ml, and poured into 30 ml of 50% sulfuric acid; here the sulfate of 2,4,5-triamino-6-hydroxypyrimidine with one mole of crystallization water crystallized rapidly. In this way over 95% of the 2,4,5-triamino-6-hydroxypyrimidine present in the reaction solution was isolated; the substance remaining in solution was not included in calculating the yields.

In alkaline medium the electroreduction of 5 g of 2,4-diamino-5-isonitroso-6-hydroxypyrimidine dissolved in 60 ml of 1% sodium hydroxide solution was run with stirring in a 110 ml diaphragmed beaker. On conclusion of reduction the solution was filtered into 30 ml of 50% sulfuric acid, and the 2,4,5-triamino-6-hydroxypyrimidine was isolated as the sulfate.

In different experiments we studied the influence of the current density, the temperature and the cathode material, and in hydrochloric acid also the concentration of the acid, on the reaction for the electrolytic reduction of 2,4-diamino-5-isonitroso-6-hydroxypyrimidine.

Since the reduction in acid medium took place in a heterogeneous medium, then, as a rule, the experiments were run with a 100% excess of current, while in homogeneous alkaline solution it proved sufficient to use a 20% excess of the current when compared to the theoretical.

Effect of current density on yield of 2,4,5-triamino-6-hydroxypyrimidine. Varying the current density in a wide range (from 3 to 17 amp/sq dm) exerts very little effect on the yield when the reduction is run in acid medium (Table 1); reduction at 25 amp/sq dm proceeds slowly and in poor yield, which is apparently associated with a strong polarization of the cathode. In alkaline medium a change in the current density from 1 to 25 amp/sq dm is practically without effect on the yield of amino compound.

TABLE 1

Influence of Current Density on Yield of 2,4,5-Triamino-6-Hydroxypyrimidine

a) Experiments in acid medium using Pb cathode in 10% hydrochloric acid at 40°

Current density (amp/sq dm)	2	3	5	7	9	11*	17*	25*
Yield of substance (%)	65.0 (150% current)	74.0	75.1	77.5	77.4	76.5	79.2	56.6 (1000% current)

b) Experiments in alkaline medium using a Pb cathode at 30°

Current density (amp/sq dm)	1	2	4	6	8	10	15	20	25
Yield of substance (%)	72.0	69.5	72.0	74.4	75.3	72.0	74.0	73.3	74.7

* At a current density of 11 amp/sq dm and higher the area of the cathode used was reduced in half in order to have sufficient time to dissolve the starting product.

Influence of cathode material. The yield of 2,4,5-triamino-6-hydroxypyrimidine depends on the hydrogen overvoltage at the different metal cathodes (Pb and Zn > Cu > Fe); the low yield using a mercury cathode can be explained by its specific state. The yield of substance in alkaline medium depends but slightly on the cathode material. Using a zinc or mercury cathode the yield of substance is found to depend directly on the amount of electricity passed through.

Electroreduction with the addition of either tin or zinc salts, used as promoters, led to a slight (3-4%) increase in the yield of substance when a lead cathode was used.

TABLE 2

Influence of Cathode Material on Yield of 2,4,5-Triamino-6-Hydroxypyrimidine (at 40° and a Current Density of 7-8 amp/sq dm)

Cathode material	Hg	Zn	Sn	Pb	Cu	Ni	Fe
Yield of substance in 10% hydrochloric acid (in %)	47.1	80.0, 81.6, 75.1	79.5	78.0, 78.2, 77.5	70.2	69.0	65.8
Yield of substance in alkaline medium (%)	42.9 (75.5 with 200% current)	31.8 (66.8 with 200% current)	59.3	77.2	77.3	71.4	--

The experiments on the reduction of 2,4-diamino-5-isonitroso-6-hydroxypyrimidine in hydrochloric acid of variable concentration are given in Table 3.

TABLE 3

Influence of Hydrochloric Acid Concentration on Yield of 2,4,5-Triamono-6-Hydroxypyrimidine (with a Current Density of 7 amp/sq dm at a Pb Cathode)

Hydrochloric acid concentration (%)	Yield of substance (%)		
	40°	60°	80°
5	57.4	74.0	
10	78.2, 77.5	69.5, 66.8	35.8
17	66.0		
36	21.1		

The influence of temperature was studied in the experiments using a lead cathode: in 10% hydrochloric acid at a current density of 7 amp/sq dm, and in alkaline solution at a current density of 8 amp/sq dm. The results of the experiments are shown in Fig. 1.

Yield based on the current. When the reduction was run in 10% hydrochloric acid at 40° the yield based on the current was 95% (when 70% of the theoretically required amount of electricity was passed through). When the reduction was run in 5 and 10% hydrochloric acid at 60° the yield based on the current decreased to 83.5%.

The relationship between the yield based on the current and the amount of electricity passed through when the reduction is carried out in an alkaline medium is shown in Fig. 2.

As had been shown by us, because of the tendency for hydrolysis of the amino group the yield of the pyrimidine amino compound (II) is greatly reduced with increase in both acid concentration and in temperature (Fig. 1) when 2-4-diamino-5-isonitroso-6-hydroxypyrimidine (I) is subjected to electrolytic reduction in an acid medium. The optimum temperature is about 40° or slightly higher. It should be mentioned that the formed 2,4,5-triamino-6-hydroxypyrimidine is stable under the reduction conditions, and its yield remains practically constant with increase in both the current density and the amount of electricity passed through.

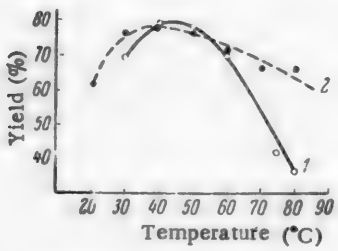


Fig. 1. Relationship between the yield of 2,4,5-triamino-6-hydroxypyrimidine and the temperature. 1) In acid medium, 2) in alkaline medium.

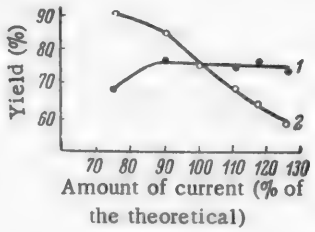


Fig. 2. Relationship between the yield of 2,4,5-triamino-6-hydroxypyrimidine and the amount of electricity (in alkaline medium, current density 6 amp/sq dm, temperature 30°). 1) yield of substance, 2) yield based on the current.

The electrolytic reduction of 2,4-diamino-5-isonitroso-6-hydroxypyrimidine (I) in alkaline medium to 2,4,5-triamino-6-hydroxypyrimidine (II) proceeds without the formation of the by-products characteristic for the reduction of nitro compounds in alkaline medium. This is due to the fact that when the electroreduction is run in alkaline medium the o-nitrosohydroxydiaminopyrimidine (I) reacts in the form of the quinone hydroxyimine, as had been shown for the catalytic reduction of this compound [2] and as is characteristic for o- and p-isonitrosophenols. The influence of the temperature factor in alkaline medium is expressed to a much lesser degree than in acid medium (Fig. 1).

A low yield of 2,4,5-triamino-6-hydroxypyrimidine in hydrochloric acid medium can be explained by the hydrolytic cleavage of the amino group from 2,4-diamino-5-isonitroso-6-hydroxypyrimidine with the formation of 2-amino-4,6-dihydroxy-5-nitrosopyrimidine [7].

SUMMARY

The electrolytic reduction of 2,4-diamino-5-isonitroso-6-hydroxypyrimidine in either acid or alkaline medium proceeds with the formation of 2,4,5-triamino-6-hydroxypyrimidine. It was shown that the material of the cathode exerts an influence on the yield based on the current when the electrolytic reduction of 2,4-diamino-5-isonitroso-6-hydroxypyrimidine is run in acid medium.

This is not observed when the electroreduction is run in alkaline medium.

LITERATURE CITED

[1] Traube, Ber. 33, 1371 (1900).

[2] V. M. Berezovskii and L. I. Strel'chunas, Trans. All-Union Vitamin Research Institute 5, 28 (1954). (State Food Industry Press for Technology and Economics).*

[3] German Patent 166,267.

[4] O. Brown and J. Warner, Trans. Electrochem. Soc. 41, 224 (1922).

[5] S. Swann, Electrolytic Methods for the Preparation of Organic Compounds [Russian translation] (IL, 1951).

[6] N. A. Izgaryshev and S. S. Kruglikov, Proc. Acad. Sci. USSR 94, 913 (1954).

[7] E. Taylor and C. Cain, J. Am. Chem. Soc. 71, 2282 (1949).

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*In Russian.

DETERMINATION OF THE NUMBER OF ELECTRONS PARTICIPATING IN THE PROCESS FOR THE REDUCTION OF STYPTICINE AT A DROPPING MERCURY ELECTRODE. II

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The basic equations of polarography can be used for the determination of the number of electrons participating in a reaction at the dropping-mercury electrode. However this method is not applicable if the studied process is irreversible. A number of papers have been published in recent years on determining the number of electrons participating in an electrode reaction with the aid of coulometric methods [1-6]. A method that is extremely convenient and simple in this respect is that of polarographic coulometry, the essence of which is that the amount of reduced substance is divided by the amount of electricity. The number of moles of reduced substance is determined by the decrease in the limiting current with time. Several methods can be used to calculate the number of electrons participating in the process. Because of the simplicity of the calculations, the logarithmic [5] and arithmetical mean [6] methods possess the greatest interest.

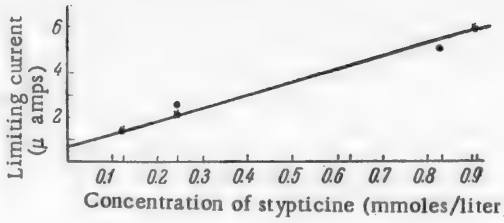
To calculate the number of electrons n by the logarithmic method it is convenient to use the formula

$$n = \frac{I_0}{c_0} \cdot \frac{K}{222 \cdot 10^3 \cdot v}, \qquad (1)$$

where: I_0 is the limiting current (in μ amp), c is the initial concentration of the substance (in mmole/liter), v is the electrolyte volume (in ml), and $K = \frac{t}{\log \frac{h_0}{h_t}}$. The value K is obtained by the following transformations. Taking into consideration that $\log \frac{I_0}{I_t} = \frac{1}{K} \cdot t$ [5], we find that $K = \frac{t}{\log \frac{I_0}{I_t}}$, while on the basis of the equality of the ratios $\frac{I_0}{I_t} = \frac{h_0}{h_t}$, where: h is the height of the polarographic wave (in mm), and t is the time (in sec), we find that $K = \frac{t}{\log \frac{h_0}{h_t}}$. The formula used for calculation by the arithmetical mean method can be depicted in the following form

$$n = \frac{M}{F} \cdot t \cdot \frac{h_0 + h_t}{h_0 - h_t} \cdot \frac{I_0}{2vc}, \qquad (2)$$

where: M is the molecular weight of the reacting substance, F is 96,500 coulombs, t is the time (in sec), h_0 and h_t are the heights of the polarographic wave (in mm), I_0 is the limiting current (in μ amp), v is the volume (in ml), and c is the concentration (in μ g/ml).



Linear relationship existing between the value of the limiting current and the concentration of stypticine in solution at pH 8.02 and 2.61.

The arithmetical mean method of calculation makes it possible to check in a simple manner the calibration of the mirror galvanometer – a necessary value for obtaining a true diffusion current in μ amps.

The method of polarographic coulometry was checked by us on the examples of determining the number of electrons participating in the process for the reduction of p-nitroaniline, cadmium nitrate, cobalt nitrate and the alkaloid stypticine at a dropping-mercury electrode, in which connection the data obtained by us for p-nitroaniline, cadmium nitrate and cobalt nitrate agree with the results of [6].

The linear relationship existing between the values of the diffusion currents and the corresponding concentration of stypticine at pH 8.02 and 2.61 is shown in the Figure.

Taking into consideration the fact that the values of the limiting currents at various pH show very little fluctuation, it is possible to calculate their mean values for each concentration and to plot them on the graph. In this case also it is possible for us to establish that a linear relationship exists between the values of the limiting currents and the concentrations of stypticine in solution, which is expressed by the equation of a straight line. It should be mentioned that Kirkpatrick [7] also established that a linear relationship exists between the value of the diffusion current and the concentration of stypticine in solution.

EXPERIMENTAL

For running the polarographic coulometry experiments we used the vessel proposed by Stromberg and Markacheva [5] and modified somewhat by us. The vessel is a glass tube with a diameter of 5-6 mm and a length of 8 cm; in its lower part the electrolyzer is connected to a small vessel, having a hollow tap for draining off the accumulated mercury. As anode we used a saturated calomel electrode, connected to the electrolyzer by a salt bridge of agar-agar and potassium chloride solution.

The experiments were run as follows. The dry electrolyzer was first filled with pure nitrogen, and then some mercury was introduced into it. The surface of the mercury in the electrolyzer was covered with 1 to 2 drops of trichloroethylene in order to protect the mercury from oxidation. A current of pure nitrogen was first passed through the investigated solution for 20 minutes. Using a microburette, exactly 0.5 ml of the investigated solution (stypticine in suitable buffer solution) was introduced into the electrolyzer. By means of a ratchet device the capillary end of the dropping electrode was immersed in the investigated solution. Then a polarization voltage of −1.3 v was applied, and the height of the diffusion current was recorded. The value of the residual current was established from a previous experiment with the buffer solution, on which ground the polarographing was run (in the proper interval of voltages). Changes in the height of the diffusion current were recorded at 10 minute intervals. The obtained readings were plotted on the graph "time–current," and the points falling on a straight line were taken for subsequent calculations. The polarographing was run for 50 minutes, the same as in the experiments of Stromberg and Markacheva [5] and of Reynolds and Shalgosky [6].

For the work we used a SGM-8 polarograph and a M21/5 magnetoelectric galvanometer. The galvanometer was previously calibrated.

The polarographic coulometry of stypticine gave the following data. The initial concentration c_0 of stypticine was equal to 2890 μ g in 1 ml, or 11.3 mmoles/liter. The initial limiting current I_0 = 249.53 μ amps, from which

$$I_0/c_0 = 249.53 : 11.3 = 22.08$$

The data for calculating according to formulas (1) and (2), both by the logarithmic and by the arithmetical method and the relationship between the limiting current and the time are given in the Table.

From the obtained data it follows that two electrons participate in the reduction of stypticine at a dropping mercury electrode. Taking into consideration the structure of stypticine, it can be assumed that this reaction goes due to involvement of the double bond of the heterocyclic ring. The presence of one wave indicates that the reduction is apparently single-stage. A two-electron wave in the reduction of stypticine (cotarnine) was also established by Coufalik and Santavy [8] using the spectrographic method.

Data for Calculating the Number of Electrons Involved in the Reduction of Stypticine at a Dropping-Mercury Electrode

Time (sec)	Diffusion current		Logarithmic method of calculation		Arithmetical mean method of calculation	
	(mm)	(μA)	$K=\frac{t}{\lg\frac{h_0}{h_t}}$	n (number of electrons)	$\frac{h_0+h_t}{h_0-h_t}$	n (number of electrons)
0	222	249.5	—	—	—	—
600	174	195.5	5668	1.13	8.25	1.13
1200	160	179.9	8427	1.68	6.16	1.69
1800	156	175.3	11749	2.34	5.72	2.35
2400	139	156.2	11805	2.35	4.35	2.39
3000	126	141.6	12369	2.46	3.62	2.43
			Average	1.992		1.998

SUMMARY

1. Using the method of polarographic coulometry it was established that two electrons are involved in the reduction of stypticine at a dropping-mercury electrode.

2. Taking into consideration the structure of stypticine, it can be assumed that this reaction goes due to involvement of the double bond in the heterocyclic ring.

LITERATURE CITED

[1] J. Lingane, J. Am. Chem. Soc. 67, 1917 (1945).

[2] M. B. Neiman, T. A. Pëtukhovskaia, A. V. Riabov and E. M. Sheianova, Factory Labs. 15, 1277 (1949).

[3] S. G. Mairanovskii and M. B. Neiman, Proc. Acad. Sci. USSR 79, 85 (1951).

[4] G. Gilbert and Rideal, Trans. Far. Soc. 47, 396 (1951).

[5] A. G. Stromberg and T. M. Markacheva, J. Phys. Chem. (USSR) 28, 671 (1954).

[6] G. F. Reynolds and K. J. Shalgosky, Anal. Chim. Acta, 10, 273 (1954).

[7] H. F. W. Kirkpatrick, Quart. J. Pharmacy and Pharmacology 18, 4 (1945).

[8] Coufalik and Santavy, Chem. Listy, 47, 1609 (1953).

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THE PREPARATION AND CERTAIN PROPERTIES OF SILICON NITRIDE

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The literature reports the presence in the silicon–nitrogen system of three chemical compounds: Si_3N_4, Si_2N_3 and SiN [1]; the only nitride whose existence has been definitely established, however, is Si_3N_4, which contains 39.8% nitrogen. According to the data in [2], obtained by x-ray and electron diffraction analysis, Si_3N_4 has a rhombic lattice (isomorphous with Ge_3N_4) with spacings a = 13.38 ± 0.03, b = 8.60 ± 0.2, c = 7.74 ± ± 0.02A. The sp. gr. of the compound Si_3N_4 according to various data is equal to 3.17-3.44 g/cc [3], m. p. 1900°. The nitride is exceptionally stable chemically. Thus the following reagents had no effect upon it in tests of 500 hours duration: HCl, H_2SO_4, HNO_3, H_3PO_4 at all concentrations, chlorine (at 900°), H_2S (at 1000°), boiling 25% NaOH solution. Molten NaOH dissolves Si_3N_4. The nitride is decomposed by hydrofluoric acid solutions. Silicon nitride is very resistant to the action of molten metals: aluminum at 1000° (shows no decomposition after 100 hours), lead at 400° (144 hours), tin at 300° (144 hours), zinc at 550° (500 hours), magnesium at 750° (20 hours); the nitride is corroded appreciably in contact with molten copper [3].

The stability toward oxidation in air, expressed as the increase in weight on unit surface after oxidation for 2 hours, is 5.0 mg/cm^2 for Si_3N_4, compared with, for example, 10.0 mg/cm^2 for TiB_2 and 42.5 mg/cm^2 for hot-pressed titanium carbide.

A number of methods have been proposed for the preparation of silicon nitride: direct combination of elemental silicon with nitrogen [1, 4], heating a mixture of silica and carbon in a current of nitrogen [1], heating silicon carbonitride in a current of nitrogen [5], ignition of triimidodisilene [1] and a number of others [6, 8].

In the present work the preparation of Si_3N_4 was checked using two of the methods given in the literature – by nitriding a mixture of silica and carbon and by the direct nitriding of elemental silicon. Certain properties of this compound have also been studied.

Nitriding a Mixture of Silica and Carbon

The composition of the charge was calculated from the equation $3SiO_2 + 6C + 2N_2 = Si_3N_4 + 6CO$. The charge was prepared by mixing SiO_2 and finely divided carbon in steel drums for 6 hours and afterwards sifting 3 times through a coarse sieve (20 mesh). The charge was heated in small graphite boats in a graphite tube furnace to 1000-1800°, the temperature being maintained constant for one hour every 100°.

It was established by chemical analysis of the specimens that at all temperatures the predominant reaction is the formation of silicon carbide, whose concentration in the products of the nitriding process amounts to 15% at 1400° and up to 85% at 1800°; the concentration of nitrogen does not exceed 0.5 + 1.5%, i.e., the yield of Si_3N_4 is equal to 2-4%.

Nitriding Silicon Powder

The reaction was carried out in a TVV-2 furnace with tungsten heater, using elemental silicon powder of 99.92% purity (the particle size did not exceed 40 μ). The nitrogen was first purified from oxygen and moisture by the usual method – a 2-fold passage through a column of copper turnings at 540° and a 2-fold dehydration with phosphorus pentoxide. The nitrogen was not analyzed after it had been thus purified; the agreement between the sum of the concentrations of Si + N and 100% in the specimens obtained in the nitriding process, however, indicates that it was sufficiently pure. Twenty g samples of the silicon powder were placed

TABLE 1

Nitriding Silicon Powder

Temperature		$\frac{1}{T} \cdot 10^3$	N concentration (%)	Phase composition	Lattice spacing (A)				Reaction constant K (g/cc · sec.)	log K
					Si-phase	Si_3N_4-phase				
°C	°K				a	a	b	c		
742	1015	0.988	0	Si	5.41_8	—	—	—	—	—
826	1099	0.914	0	Si	5.41_7	—	—	—	—	—
910	1163	0.846	0	Si	5.41_9	—	—	—	—	—
970	1243	0.805	0.29	Si + Si_3N_4	5.41_9	—	—	—	$7.49 \cdot 10^{-7}$	—6.1255
1004	1277	0.785	6.45	Si + Si_3N_4	5.41_9	—	—	—	$2.94 \cdot 10^{-6}$	—5.5317
1130	1403	0.712	15.94	Si + Si_3N_4	5.41_8	13.37_5	8.59_8	7.74_5	$1.88 \cdot 10^{-5}$	—4.7258
1216	1489	0.672	26.35	Si + Si_3N_4	5.41_4	13.38	8.60_0	7.74_6	$4.15 \cdot 10^{-5}$	—4.3820
1400	1673	0.597	37.31	Si + Si_3N_4	5.41_9	13.38_3	8.59	7.74_1	$9.61 \cdot 10^{-5}$	—4.0173
1490	1763	0.568	38.32	Si + Si_3N_4	5.41_8	13.37_9	8.59_9	7.74_1	$2.00 \cdot 10^{-4}$	—3.6990
1600	1873	0.536	39.71	Si + Si_3N_4	5.41_9	13.38_5	8.59_7	7.74_1	$3.32 \cdot 10^{-4}$	—3.4769

in corundum crucibles. With a constant pressure of nitrogen of 1 atmosphere, the temperature was raised to the required value in 10 minutes, after which this temperature was maintained for 0.5-20 hours until the silicon had been completely saturated with nitrogen at the required temperature. The appropriate data for several temperatures are given in Fig. 1.

It should be noted that the corundum crucibles do not react at all with the silicon, since in the very first moments of the action of the nitrogen on the silicon powder, each particle becomes covered with a compact film of refractory nitride, and further transfer of the nitrogen to the silicon is brought about by a diffusion process (transmission diffusion through the layer.) Thus from the very beginning of the nitriding process, in the 10-minute interval in which the temperature is being raised, the silicon is enveloped in a refractory covering of silicon nitride which does not react with the Al_2O_3 or other material in the crucibles up to high temperatures.

The temperatures in the furnace during the experiments were measured up to 1300° using a platinum platinorhodium thermocouple, and above this temperature using an optical pyrometer graduated by means of the platinum platinorhodium thermocouple under conditions corresponding to the working conditions, which made it necessary to introduce corrections for the absorption of the medium, the quartz window, etc.

The technical experiments carried out on the saturation of silicon powder with nitrogen were not undertaken for the purpose of making a complete study of the equilibrium and kinetics of the nitriding reaction $3Si + 2N_2 \rightleftharpoons Si_3N_4$; they may, however, give approximate values for the constant for this reaction and for the energy of activation for the diffusion formation of the nitride phase Si_3N_4, which was identified in all the specimens from 970° onward by x-ray structural examination. This was carried out by photographing the specimens, obtained during the nitriding process, in a camera of 85.78 mm diameter using Cu Kα-radiation with a Ni filter and an exposure of 10-12 hours. The x-ray diffraction patterns for Si_3N_4 are very complex and contain approximately 110 lines. The most intense lines, with $\underline{d}$ equal to 0.9497, 0.9515, 0.9620, 0.9710 and 0.9827, were chosen for the calculation of the lattice spacing.

From the data obtained, which are given in Table 1, we may reach the preliminary conclusion that nitrogen has either no solubility, or very slight solubility, in silicon, and that there is no appreciable range of homogeneity of the Si_3N_4 phase. It should be noted that the x-ray diffraction patterns showed no other

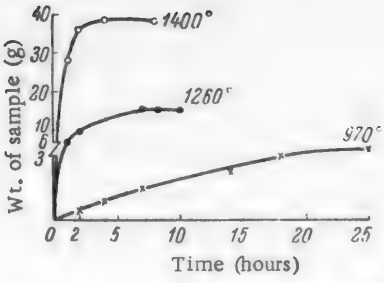

Fig. 1. Curves showing the saturation of silicon with nitrogen.

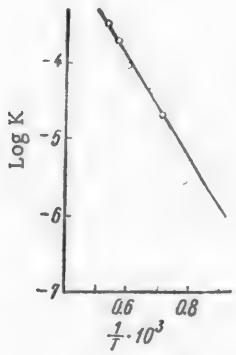

Fig. 2. The relationship between the logarithm of the nitriding reaction constant and the temperature.

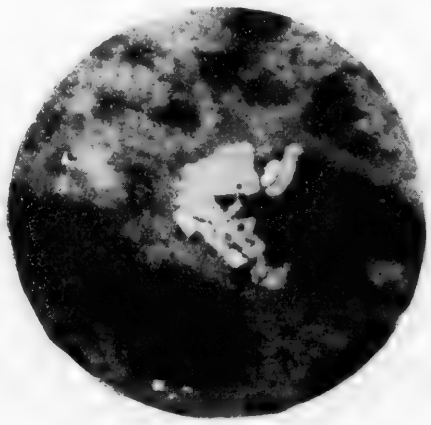

Fig. 3. Photomicrograph of nitrided area in silicon powder (×660).

phases than Si and Si_3N_4, which renders doubtful the existence of the phases SiN and Si_2N_3 reported in the literature. The "SiN phase" may be taken from the results of chemical analysis of the mixture Si + Si_3N_4; as regards the "Si_2N_3 phase," it is difficult to account for its detection in certain older works.

From the data giving the increase in weight during the absorption of nitrogen, using the method adopted by Gulbransen and his school [7], we calculated approximate values for the nitriding reaction constant,

$$K = \frac{\Delta p}{v\tau}$$

where: Δp – increase in weight in the nitriding process (g), v – volume of silicon before the nitriding process (cc), τ – saturation time at constant temperature (seconds.)

The numerical values for the reaction constant, calculated according to the formula, are given in Table 1 and have been used to construct the curve given in Fig. 2.

It should be noted that the nitriding process at temperatures above 1600° gives lower increases in weight, while at 1820° there is no increase in weight at all. This cannot be explained by volatilization of the silicon, since the silicon particles, as pointed out above, are covered with a refractive layer of Si_3N_4. This last circumstance also apparently explains the fact that a change in the state of aggregation of the silicon at 1423° has no appreciable influence on the rate of reaction. It must therefore be assumed that at temperatures above 1600°, either Si_3N_4 is not formed at all or else its rate of dissociation is greater than its rate of formation. From this it may be concluded that the dissociation pressure of Si_3N_4, given in the literature as equal to 1 atmosphere at 1977°, is somewhat low; a dissociation pressure equal to 1 atmosphere is reached at a temperature of the order of 1780-1820°.

The energy of activation for the diffusion of nitrogen into silicon with the formation of the phase Si_3N_4 has been calculated from the values of the reaction constant for the nitriding process and found to be equal to 33800 ± 719 cal/mole.

The nitride formed in the nitriding process has a well-defined crystalline structure (Fig. 3) with a particle size of 10-15 μ; the microhardness of the Si_3N_4 crystals (determined using a PMT-3 apparatus with an indenter load of 60 g) is equal to 3337 ± 120 kg/mm². The microhardness of the inclusions of the silicon phase is equal to approximately 900 kg/mm². It is practically equal to the hardness of the original

silicon powder, which provides confirmation that nitrogen is insoluble or only very slightly soluble in silicon.

Compression of silicon nitride powder at pressures as low as 6 tons/cm^2 leads to the formation of stable briquets with a density of 2.72-2.74 g/cc (i.e., with 20-25% of pores.) Further increase in the pressure at which compression takes place causes considerable internal stress and leads to a consequent reduction in the density of the briquets when the pressure is removed. The shape of the compression curve obtained (Fig. 4) is characteristic of powders of hard brittle materials with a low plasticity.

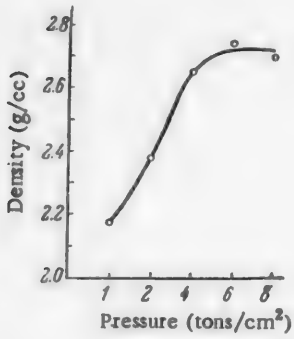

Fig. 4. The relationship between the density of silicon nitride briquets and the pressure used for compression.

It is of some interest to compare the properties of silicon boride, carbide and nitride, which are given in Table 2 [3, 4, 8].

Without taking into account the influence of the difference in the crystal structures, it may be suggested that in the series Si—B, Si—C and Si—N there is a change in the nature of the bond between the silicon and the metalloid from metallic to covalent. Boron and silicon, which have similar ionization potentials, undoubtedly form a common electronic association of the weakly-bound electrons which take part in the transfer of current. In silicon carbide, there is still preserved, in addition to the strong covalent bonds, a bond of the metallic type, which is responsible for the fairly low electrical resistance. The most clearly defined compound of the type with covalent bonds is silicon nitride, which in this series shows the greatest brittleness (with the lowest hardness) and electrical resistance, together with the lowest melting point and coefficient of thermal expansion. The activation energy of the formation by diffusion of the phases should evidently decrease in the order Si—N, Si—C and Si—B.

TABLE 2

A Comparison of the Properties of Silicon Boride, Carbide and Nitride

Property	SiB_3	SiC	Si_3N_4
Melting point (or dissociation temperature) (°C)	2750°	2600°	1900°
Microhardness in kg/mm^2 (with	5352 ± 167	3340	3337 ± 120
Modulus of elasticity (kg/mm^2)	—	2900—4700	11600—14500
Specific resistance (in Ω · cm)	Good conductor of electricity	50	$1.426 \cdot 10^3$
Coefficient of thermal expansion	—	$4.86 \cdot 10^{-6}$	$2.75 \cdot 10^{-6}$

SUMMARY

1. A study has been made of the conditions for nitriding elemental silicon at 970-1600°. Approximate values have been obtained for the reaction constant for the nitriding process and for the energy of activation of the reactive diffusion of nitrogen into silicon with the formation of the phase Si_3N_4, which is equal to 33800 ± 719 cal/mole.

2. The microhardness of Si_3N_4 has been determined and found to be equal to 3337 ± 120 kg/mm^2; it has been established that the solubility of nitrogen in silicon is small and that there is no range of homogeneity of the phase Si_3N_4.

LITERATURE CITED

[1] K. S. Evstrop'ev and N. A. Toropov. The Chemistry of Silicon and the Physical Chemistry of the Silicates• (1952).

[2] W. Leslie, K. Caroll and R. Fischer, J. Metals 4, 204 (1952).

[3] J. Collins and R. Gerby, J. Metals 7, 612 (1955).

[4] L. Weiis and T. Engelhardt, Z. anorg. Ch. 65, 38 (1910).

[5] W. F. Schutzenberg and L. Kolson, Compt. rend. 92, 32 (1892).

[6] L. Blix and Birbelauer, Ber. 36, 4220 (1903).

[7] E. Gulbransen and K. Andrews, J. Metals 187, 741 (1949); 188, 586 (1950).

[8] G. V. Samsonov and V. P. Latysheva, Proc. Acad. Sci. USSR 105, 499 (1955).

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THE ELECTROLYTIC REDUCTION OF THORIUM TETRACHLORIDE IN SALT MELTS

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Until recently it was considered that thorium could only have a valence of four in its compounds. In connection with the problem of the placing of the actinide elements in the periodic system of the elements, studies have been made on the preparation of thorium compounds of lower valence. In the literature of recent years there are reports [1-3] that at increased temperatures (of the order of 500-600°), either by synthesis from the elements, or by the reaction between the metal and the tetrahalide, it has been possible to prepare halogen derivatives of di- and trivalent thorium. The lower compounds of thorium are very reactive. They exhibit powerful reducing properties; they react with the glass walls of containing vessels, forming compounds of the type $ThOX_2$; and they react with water with the formation of Th^{4+} and evolution of hydrogen.

At temperatures above 600° the lower halogen derivatives of thorium decompose according to the equations:

$$2ThX_3 \rightarrow ThX_4 + ThX_2$$
$$2ThX_2 \rightarrow ThX_4 + Th.$$

It has been shown by work in our laboratory that metallic thorium in salt melts reduces Th^{4+} ions to lower valence states. The reduction stops at the stage of Th^{2+} formation. The lower chlorides, being dissolved in the melt, are not decomposed to an appreciable extent even at a temperature of the order of 900°.

In one of our previous works [4] on the study of cathodic processes in the electrolysis of chloride melts containing Th^{4+} ions, it was established that lower chlorides of thorium are intermediate products in the electrolytic preparation of the metal. As laboratory experiments show, thorium, during the electrolysis, does not begin to be deposited immediately, but only after a certain "critical" value for the cathodic current density has been reached. At current densities lower than this limiting value the process taking place involves only a change in the charge of the Th^{4+} ions to Th^{2+} and Th^{3+}.

It is thus possible to prepare lower chlorides of thorium by an electrochemical method in salt melts by electrolysis at low current densities.

It has proved of interest to make a more detailed study of the conditions for the electrochemical reduction of thorium in salt melts and, in particular, to study the properties of an electrolyte containing an appreciable quantity of lower valence thorium ions.

Melts containing Th^{2+} and Th^{3+} exhibit powerful reducing properties. Considerable difficulties in this connection had to be overcome in the search for a suitable material for the preparation of the cell and the creation of an inert atmosphere.

The materials usually employed for the preparation of electrolytic cells – glass, quartz, porcelain and even alundum – proved to be unsuitable for our experiments. The relatively small quantities of Th^{3+} and Th^{2+} ions which enter the melt during the electrolysis are very rapidly lost as a result of reaction with the material of the cells walls.

It can be shown on the basis of existing thermodynamic data that Th^{2+} will reduce aluminum oxide at the temperature of the experiment (700°): $2Al_2O_3 + 6ThCl_2 \rightleftarrows 4Al + 3ThO_2 + 3ThCl_4$, the change in the isobaric potential for this reaction being

$$\Delta Z = 49.100 - 118.2T \text{ cal/mole}$$

from which

$$\Delta Z \leq 0 \quad \text{at} \quad T \geq 500°.$$

This reaction, however, could not be materially reflected in the previous studies on the reduction of the tetrachloride by metallic thorium in melts, since a fairly massive piece of metallic thorium was taken for the experiments and the process by which the thorium entered the melt according to the reaction:

$$Th^{4+} + Th \rightarrow 2Th^{2+}$$

compensated for the slower removal of Th^{2+} ions from the melt as a result of their reaction with the walls of the cell.

We also tested several metals as materials for the preparation of a cell. Pt and Ta gave unsatisfactory results. Crucibles prepared from these metals gave a considerable loss in weight after electrolysis and were extensively destroyed on their surfaces. In this case, in all probability, interaction leads to the formation of alloys of thorium and the corresponding metal.

The most suitable material for the preparation of the crucible in which the electrolysis was carried out proved to be metallic molybdenum. Its surface after the electrolysis showed no visible alteration, and the weight remained constant. All the experiments on the study of the electrolytic reduction of $ThCl_4$ in salt melts were therefore carried out in molybdenum crucibles.

The lower chlorides of thorium are very sensitive even to traces of oxygen. The argon with which the cell was filled was therefore carefully purified. For this purpose the gas was passed in turn through a tube filled with calcium (500°), then through turnings of metallic magnesium (450°), and finally through a tube containing metallic titanium in a furnace (500°). As a measure of the purity of the gas it was observed that after the electrolysis, which lasted for a considerable time (5-6 hours), the surface of the molybdenum crucible had undergone no visible change. The crucible did not lose its characteristic metallic luster.

The construction of the cell in which the studies were carried out is represented diagramatically in Fig. 1. The melt containing the thorium tetrachloride was placed in the molybdenum crucible, which also served as the cathode. A hollow carbon tube was used as the anode. In order to prevent the chlorine liberated at the anode from entering the electrolyte containing the reduced species, the anode region was separated from the cathode region by an asbestos diaphragm. At the same time the anode was placed in a separate quartz tube, into the foot of which was sealed a capillary packed with asbestos.

The electrolysis for the preparation of the lower chlorides of thorium was carried out at a temperature of 700° in a melt of alkali metal chlorides containing 16.1% by weight of $ThCl_4$. The current density was of the order of 0.001-0.008 amp/cm^2. The time of electrolysis depended on the value of the current density.

Results and Discussion

As the reduced species accumulate, the melt becomes darker and darker, the lower chlorides of thorium giving it a grey coloration. If such a melt, containing an appreciable amount of the chlorides of di- and trivalent thorium, is brought into contact with air, oxidation takes place very violently with flashes of combustion, the whole melt sparkles and crackling noise is heard.

In order to confirm the reducing properties of the melt containing the lower chlorides of thorium qualitatively, it was cooled in an inert atmosphere, after which the solid ash-like mixture was treated with $FeCl_3$ and the presence of the reduced species established by back-titration with a dilute solution of $K_2Cr_2O_7$. Since oxygen, dissolved in the water, is introduced with the $FeCl_3$ solution, no definite conclusions can be reached concerning the quantitative relationships.

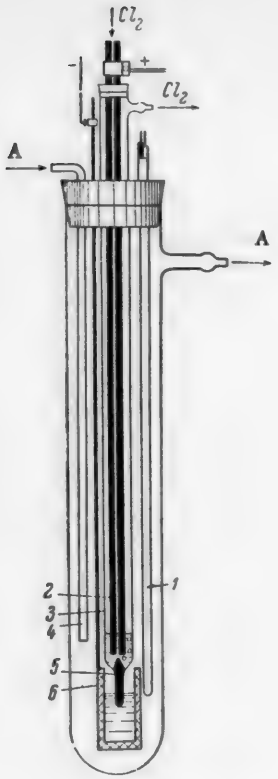

Fig. 1. The cell. 1) Thermocouple, 2) carbon anode, 3) quartz tube, 4) tube for passing in the argon, 5) asbestos diaphragm, 6) molybdenum crucible with current lead (cathode).

In order to estimate the quantitative changes taking place in the melt during the electrolysis, we measured the oxidation-reduction potentials of the system. The potential of an inert molybdenum electrode (the cathode) was recorded every 10-15 minutes using an oscillograph. The anode was used as reference electrode. At the moment when the potential was being measured, the electrolysis circuit was broken. In order to ensure that there was no change in the potential of the reference electrode at the moment when the circuit was broken, additional chlorine, prepared by the electrolysis of lead chloride, was bubbled through it.

As the measurements showed, the potential of the inert electrode during the course of the electrolysis changes according to the equation:

$$E = E_0 + \frac{RT}{2F} \ln \frac{a_{Th^{4+}}}{a_{Th^{3+}}},$$

where aTh^{4+} and aTh^{3+} = the activities of the Th^{4+} and Th^{3+} ions. In our experiments the concentrations of the ions may be used in the equation instead of the activities, since studies in our laboratory have shown [5] that melts containing less then 25% by weight of $ThCl_4$ behave as ideal solutions.

The values obtained were used to construct curves showing the change in the oxidation-reduction potential of the Th^{4+}/Th^{3+} system with time (with $\underline{i}$ = constant.) The measurements were carried out for three values of the current strength: 0.01, 0.05 and 0.1 amp. Figure 2 shows the corresponding curves. Examination of the curves reveals the presence of a number of characteristic regions. This in all probability indicates the stepwise nature of the process of reduction of the Th^{4+} ions.

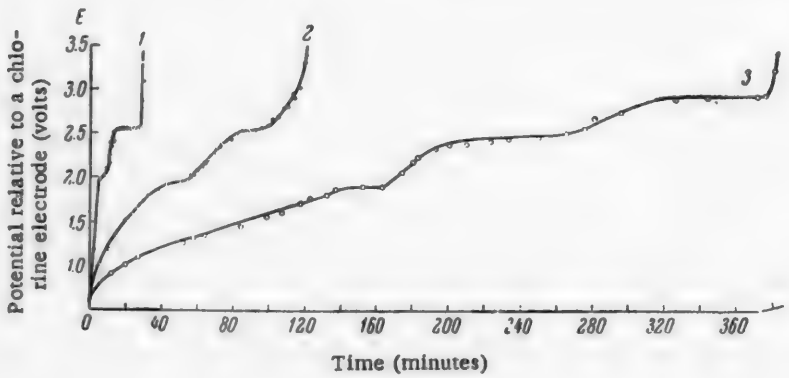

Fig. 2. Polarization of an inert electrode (the cathode) in a molten equimolar mixture of potassium and sodium chlorides containing 16.1% by weight of $ThCl_4$ at 700°. Current strength (in amp.) 1) 0.1, 2) 0.05, 3) 0.01.

Taking account of the fact that the reduction at the cathode takes place with 100% yield, it is possible to calculate the quantity of electricity which must be passed in order to reduce all the Th^{4+} ions present in the melt to the di- or trivalent state, and then to metallic thorium. As the calculations show, the quantity of electricity required theoretically for the reduction of the Th^{4+} to the lower valence states is close to the values obtained in practice.

SUMMARY

1. A study has been made of the electrolytic reduction of thorium tetrachloride at the cathode in melts of alkali metal chlorides containing 16.1% by weight of $ThCl_4$ at 700°.

2. It has been established that thorium, in its lower valence states, reacts vigorously not only with silicate materials (quartz, glass, porcelain, alundum), but also with a number of metals (Pt and Ta), as a result of the formation of the corresponding alloys with thorium.

LITERATURE CITED

[1] Jantsch, Homayr and Zemek, Monatsh. 85, 526 (1954).

[2] E. Hayek, T. Rehner and A. Frank, Monatsh. 82, 575 (1951).

[3] F. Anderson and R. D'eye, J. Chem. Soc. 1949 (Suppl. Issue. No. 2), 244.

[4] M. V. Smirnov and L. D. Iushina, Bull. Acad. Sci. USSR, Div. Chem. 1073 (1956). *

[5] M. V. Smirnov and L. E. Ivanovskii, J. Phys. Chem. 31, 641 (1957).

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ELECTROLYTIC DISSOCIATION IN NONAQUEOUS SYSTEMS

VI. SYSTEM ALLYL MUSTARD OIL–o-TOLUIDINE

S. P. Miskidzh'ian

As is known, the reaction of allyl mustard oil with amines yields substituted thioureas [1], which are not electrolytes. On the other hand, it was shown that systems, prepared from allyl mustard oil and an aromatic amine (aniline, o-toluidine, etc.), are good conductors of an electric current. The specific electroconductivity of such systems reaches the order of $10^{-3}\Omega^{-1}cm^{-1}$ [2, 3]. It is difficult to explain the presence of a high electroconductivity if it is assumed, in accord with general opinion, that the reaction products of allyl mustard oil with amines are simply substituted thioureas.

In a number of papers published by us [4, 5] it has been shown that in such systems, together with the formation of the substituted thiourea, the allyl-amine thiocyanate is also obtained; this is an electrolyte and responsible for the high electroconductivity shown by the solutions. In the indicated papers we have given the mechanism for the electrolytic dissociation of these compounds, the anion of which in all cases is SCN^-. In this paper we communicate the results obtained in studying the system allyl mustard oil–o-toluidine.

The fusion, viscosity, density, surface tension and electroconductivity properties of this system have been studied by N. A. Trifonov, K. I. Samarina and co-workers [2]. The diagrams for all of these properties show a singular point and clearly indicate that the components of this system react vigorously with each other to yield allyl-o-tolylthiourea. According to the data of the authors mentioned, the specific electroconductivity isotherm has two maxima and one minimum, found at 50 mole %, i.e., corresponding to the composition of this compound.

The maximum specific conductivity κ_{50} reaches a volume of $1.69 \cdot 10^{-3}$. Neither allyl mustard oil, nor o-toluidine, nor (especially) allyl-o-tolythiourea, the latter being the main reaction product of the indicated components, are electrolytes nor can they create such a high electroconductivity in the system. It would be natural to assume here the allyl-o-toluidine thiocyanate, which is an electrolyte and determines the comparatively high electroconductivity shown by the solution, is formed, together with substituted thiourea, as in the systems studied earlier by us.

It is our opinion that an investigation of similar systems could possess some practical value, since the allyl-amine thiocyanates are salts of ammonium bases, which in recent years are widely used in medicine as bactericidal and ganglion-blocking agents.

EXPERIMENTAL

Allyl mustard oil was obtained by the earlier described method [4]. The o-toluidine after long standing over potassium hydroxide was distilled, and for our work we took the fraction with b. p. 196-197° (746 mm), d_{20} 0.9990, n_D^{20} 1.5735. The prepared mixtures were kept in sealed ampoules in the dark. Despite, this most of the mixtures turned brown on long standing (about 1 year). The mixtures containing from 30 to 60 mole % o-toluidine solidified completely, while the mixtures containing 20, 70 and 80 mole % o-toluidine showed a crystalline precipitate after several days.

As was true of systems we studied earlier, all of the solutions of the present system showed the presence of SCN^- ion by the usual qualitative tests ($FeCl_3$, etc.).

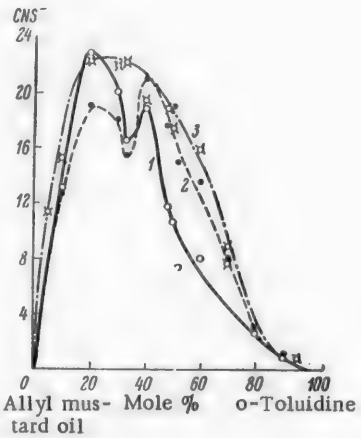

Fig. 1. Relationship between the SCN^- concentration (in weight % on the compound having SCN^- as the anion) and the composition of the mixtures of the system. 1) When the mixtures were stored for 13 months, 2 and 3) after the mixtures were heated for 28 and for 94 hours.

In this connection we decided to determine the SCN^- concentration as a function of the composition of the system. A photoelectrocolorimeter was used as the measuring device (for a detailed description of the method see [5]). The relationship between the SCN^- concentration (in weight % on the compound having SCN^- as the anion) and the composition of the mixtures, which were stored for 13 months, is shown in Fig. 1.

Earlier in studying similar systems we had observed that heating the mixtures leads to increasing the SCN^- concentration in them. For this reason we subjected all of the solutions of the present system to prolonged heating in a thermostat at 100 ± 5°. The relationships between the SCN^- concentration and the composition when the heating time was 28 and 94 hours are also shown in Fig. 1.

According to the data of [2], the mixture containing 80 mole % allyl mustard oil shows an extremely high electroconductivity. As is not difficult to see, on the SCN^- concentration–composition diagram the maximum SCN^- concentration corresponds to this composition. This fact and some other experimental data, which will be discussed below, make it possible to assume that also in the given system the reaction of allyl mustard oil with o-toluidine gives, parallel with the formation of allyl-o-tolylthiourea, a certain amount of allyl-o-toluidine thiocyanate according to the reaction $CH_3C_6H_4NH_2 + CH_2 = CHCH_2NCS \rightleftharpoons [CH_3C_6H_4\overset{+}{N}H_2CH_2CH{=}CH_2][S\overline{C}N]$. This last substance is an electrolyte; in its own medium, and also with an excess of the components present, it dissociates into ions.

As can be seen from Fig. 1, the amount of allyl-o-toluidine thiocyanate in some of the mixtures reaches 22.8%, which shows that the side reaction reaches substantial proportions in the indicated mixtures. A long heating of the mixtures does not lead to a substantial increase in the SCN^- concentration, as was observed in the systems studied by us earlier [5]. A possible explanation for this is the fact that, in contrast to the previous systems, we measured the SCN^- concentration in the present system some time (more than a year) after the preparation of the mixtures, i.e., after the reaction for the formation of allyl-o-toluidine thiocyanate was practically complete.

In studying the system allyl mustard oil–aniline [5] we were able to show that the allylphenylthiourea formed in the system is converted to allyl-aniline thiocyanate on long heating. To determine if a similar transformation also occurred in the present system, we prepared a mixture containing 50 mole % allyl mustard oil and 50 mole % o-toluidine. This mixture turned completely solid after several days, forming mainly allyl-o-tolylthiourea and a small amount of allyl-o-toluidine thiocyanate. The latter substance is responsible for the substantial electroconductivity (according to our measurements $\kappa_{70} = 2.8 \times 10^{-4}$) and brown color shown by the mixture. After repeated washing with ethyl alcohol of the solidified mixture obtained by us, followed by recrystallization, we obtained the pure allyl-o-tolylthiourea as a colorless crystalline substance with m. p. 92° and $\kappa_{100} = 2.7 \times 10^{-6}\ \Omega^{-1}\ cm^{-1}$. The allyl-o-tolylthiourea obtained in this manner was then heated for a long time in a sealed ampoule (for 10 days) at 100 ± 5°. After this length of heating the mixture was shown to contain up to 8.5% of allyl-o-toluidine thiocyanate.

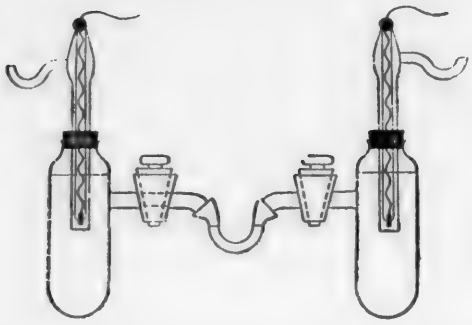

Fig. 2. Electrolysis apparatus. Explanation in the text.

To isolate the allyl-o-toluidine thiocyanate from the prepared mixtures we made use of the fact that it is readily soluble in hot water. Therefore, the compound in which we were interested was extracted with hot water until the aqueous extract failed to give a positive test for SCN^- ion. After extraction, a certain amount of tarry substance remained on the bottom of the extraction flask. A cloudiness (mainly allyl-o-tolylthiourea) appeared in the aqueous extracts on cooling. After the water extracts were filtered through several layers of dense filter paper the water was completely removed from the filtrate by distillation, first at atmospheric pressure and then in vacuo (10-20 mm). Here a very thick brown liquid which remained in the flask contained 70-73% of allyl-o-toluidine thiocyanate.

This liquid was subjected to electrolysis in the apparatus shown in Fig. 2. The investigated substance was contained in the lower part of the bend in the U-shaped tube. All of the remaining volume of the apparatus was filled with distilled water. In this way both the anodic and cathodic areas contain nothing else but water, which eliminates the progress of side electrochemical processes at the electrodes during the passage of a current and simplifies the subsequent analysis of the anolyte and catholyte. With such a construction of the apparatus the transfer of substances into the anodic and cathodic areas due to diffusion is excluded, or at least reduced to a minimum. The electrolysis was conducted at a voltage of 400-500 v. Here the current (intensity) at the start of experiment did not exceed 0.2-0.5 milliamp, but then it gradually rose and at the end of experiment reached 10 milliamps.

During electrolysis the SCN^- ions migrate to the anode, which is confirmed by the test with $FeCl_3$. Neutralization of the anolyte with KOH solution, followed by evaporation, left a crystalline substance which proved to be potassium thiocyanate.

Evaporation of the catholyte in vacuo (10-20 mm) left a viscous brown liquid. When dissolved in water this liquid showed strongly alkaline.

The experiments made with the electrolyzer support the formation of allyl-o-toluidine thiocyanate when allyl-o-tolylthiourea is heated, and its dissociation into the ions SCN^- and $[CH_3C_6H_4NH_2CH_2CH{=}CH_2]^+$.

SUMMARY

1. It was shown that the reaction of allyl mustard oil with o-toluidine yields, together with allyl-o-tolylthiourea, allyl-o-toluidine thiocyanate.

2. The abnormally high specific electroconductivity shown by the system allyl mustard oil—o-toluidine is due to the formation of the allyl-o-toluidine thiocyanate.

LITERATURE CITED

[1] N. Zinin, Bull. phys. mathem. de l'Acad. St.-Petersburg, 10, 346 (1852).

[2] N. A. Trifonov, Bull. Perm. Biol. Res. Inst. 7, Nos. 7-8 (1931).

[3] N. K. Voskresenskaia, Sci. Repts. Saratov State Univ. 6, No. 3 (1927).

[4] S. P. Miskidzh'ian and F. N. Kozlenko, Bull. D. I. Mendeleev All-Union Chem. Soc. No. 3, 37 (1953).

[5] S. P. Miskidzh'ian, J. Gen. Chem. 26, 1046 (1956).*

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LETTER TO THE EDITOR

ENTHALPY OF FORMATION OF NICKEL CARBONYL

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In 1955 we published a paper [1] in which the enthalpy of formation of liquid nickel carbonyl was determined by the explosion method developed by us. As had been shown by us ([1], page 229), for the reaction $[Ni]_{\beta} + 4CO = Ni(CO)_4$ (liquid), $\Delta H^0_{f,298} = -47.3 \pm 1$ kcal/mole. The use of this method permitted making some important corrections in the earlier found values for the enthalpy of formation of this carbonyl.

In a paper [2] that was published at the same time as ours, two values were given for the enthalpy of formation of gaseous nickel carbonyl: $\Delta H^0_{f,298} = -36.3$ kcal/mole (indirect determination) and $\Delta H^0_{f,298} = -34.5$ kcal/mole (direct determination).

In order to compare the results given in these two papers it is necessary to take into account the value of the enthalpy of vaporization of nickel carbonyl, which in the studies of various authors varies from 6.3 to 7.2 kcal/mole [2, 3]. In reference [2] the value $\Delta H^0 = 6.5$ kcal/mole is assumed to be the most probable, taken from an old study [4]. If we proceed from later studies, where $\Delta H^0 = 6.92$ [5] and $\Delta H^0 = 7.2$ [3], then the value of ΔH^0 should be taken equal to 7.0 kcal/mole.

Next, in order to compare the values for the enthalpy of formation of nickel carbonyl, computed from the experimental values of the heats of combustion, it is necessary to operate with the same values for the enthalpies of formation of the components, entering into the equation of the reaction. But in the case of NiO some differences exist in the literature on this score. Thus, in [6] the value $\Delta H^0_{f,298} = -59.3$ kcal/mole is assumed, and in [7] the value $\Delta H^0_{f,298} = -57.3$ kcal/mole. In our paper [1] a value of -58.9 kcal/mole was assumed, and in reference [2] a value of -57.3 kcal/mole. Some critical remarks concerning study [7] were made by one of us in paper [8]. At the same time, previous determinations of this value are no more correct. Substituting in the equation ([1], page 229) the value -57.3 instead of -58.9, which is completely obligatory when the results of the two studies are compared, we obtain an average correction for the value of $\Delta H^0_{f,298}$ for $Ni(CO)_4$ (liquid), found in [1] to be equal to 1.2 kcal/mole, i.e., $\Delta H^0_{f,298} = -47.3 + 1.2 = -46.1$.

As a result, the enthalpy of formation of gaseous nickel carbonyl, computed from the enthalpy of formation of the liquid carbonyl, found in [1], is equal to $\Delta H^0_{f,298} = -47.3 + 6.5 + 1.2 = -39.6$ kcal/mole, i.e., it is 5.1 kcal/mole greater than the value found by direct determination by the British authors in [2]. If for the enthalpy of vaporization of the carbonyl we assume a value of 7.0 kcal/mole (see above), then from our data for the liquid carbonyl we obtain for the enthalpy of formation of the gaseous carbonyl $\Delta H^0_{f,298} = -39.1$ kcal/mole. This last value had already been communicated by one of us [9].

A publication by some American authors [10] appeared recently, in which the value for the enthalpy of formation of gaseous nickel carbonyl is given equal to $\Delta H^0_{f,298} = -39.1$ kcal/mole ($\pm$ 0.5 kcal).*

Since in [10] for the calculations a value of 6.5 kcal/mole was taken for the enthalpy of vaporization of the carbonyl, and a value of -57.3 kcal/mole for the enthalpy of formation of NiO, then the value of -39.1 kcal/mole found in [10] corresponds to the value of -39.6 kcal/mole found in our work. In other words, the results given by us in [1] for the determination of the enthalpy of formation fo the liquid carbonyl are fully supported by the value given in [10] for the enthalpy of formation of the gaseous carbonyl (within the accuracy limits of the determinations).

*Considering the inaccurate value of the enthalpy of vaporization of the carbonyl, the accuracy indicated in [10] is high.

However in citing our data the authors of [10] permitted two gross errors: they fail to mention either that our calculation was made for the liquid carbonyl and theirs for the gaseous carbonyl, or that several different values for the enthalpy of formation of NiO were used in the calculations given in our paper. As a result of these peculiar errors the indicated authors do not compare the values −39.6 and −39.1, but instead the values −47.3 and −39.1, and they create some baseless assumptions that such a "difference" could be due to possible errors in our work.

We would like to emphasize here that our publication [1] does not give any grounds for these errors in [10]. On page 229 [1] it is clearly stated that the value of −47.3 kcal/mole for the enthalpy of formation relates to the liquid carbonyl: the equation given for the reaction bears the designation (l) after formula of the carbonyl. In the case of the gaseous carbonyl the designation would be (g). On the same page a calculation of the heat effect for the formation of the carbonyl is given three times using the value −58.9, and not −57.3 kcal/mole, for the enthalpy of formation of NiO.

In a later paper we propose to discuss some of the other erroneous assumptions expressed in [10].

LITERATURE CITED

[1] E. I. Smagina and B. F. Ormont, J. Gen. Chem. 25, 224 (1955).*

[2] J. E. Spice, L. A. K. Staveley and G. A. Harrow, J. Gen. Soc. 1955, 100.

[3] Suginuma and Satozaki, Bull. Inst. Phys. Chem. Res. Tokyo 21, 432 (1942).

[4] Dewar and Jones, Proc. Roy. Soc. A 71, 427 (1903).

[5] J. S. Anderson, J. Chem. Soc. 1930, 1653.

[6] F. D. Rossini, D. D. Wagman, W. H. Evans, S. Levine and I. Jaffe, Selected Values of Chem. Thermod. Propert. Circul of the N. B. Stand., No. 500 (1952).

[7] B. J. Boyle, E. G. Kind and K. C. Conway, J. Am. Chem. Soc. 76, 3835 (1954).

[8] B. F. Ormont, J. Phys. Chem. (USSR) 30, 1896 (1956).

[9] B. F. Ormont, "Structure and Stability of Metal Carbonyls" [in Russian]. Paper delivered at the 7th All-Union Conference on Complex Compounds (Leningrad, Oct. 13, 1956).

[10] A. K. Fischer, F. A. Cotton and G. Wilkinson, J. Am. Chem. Soc. 79, 2044 (1957).

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SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.– Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Meteorology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. – Publisher.